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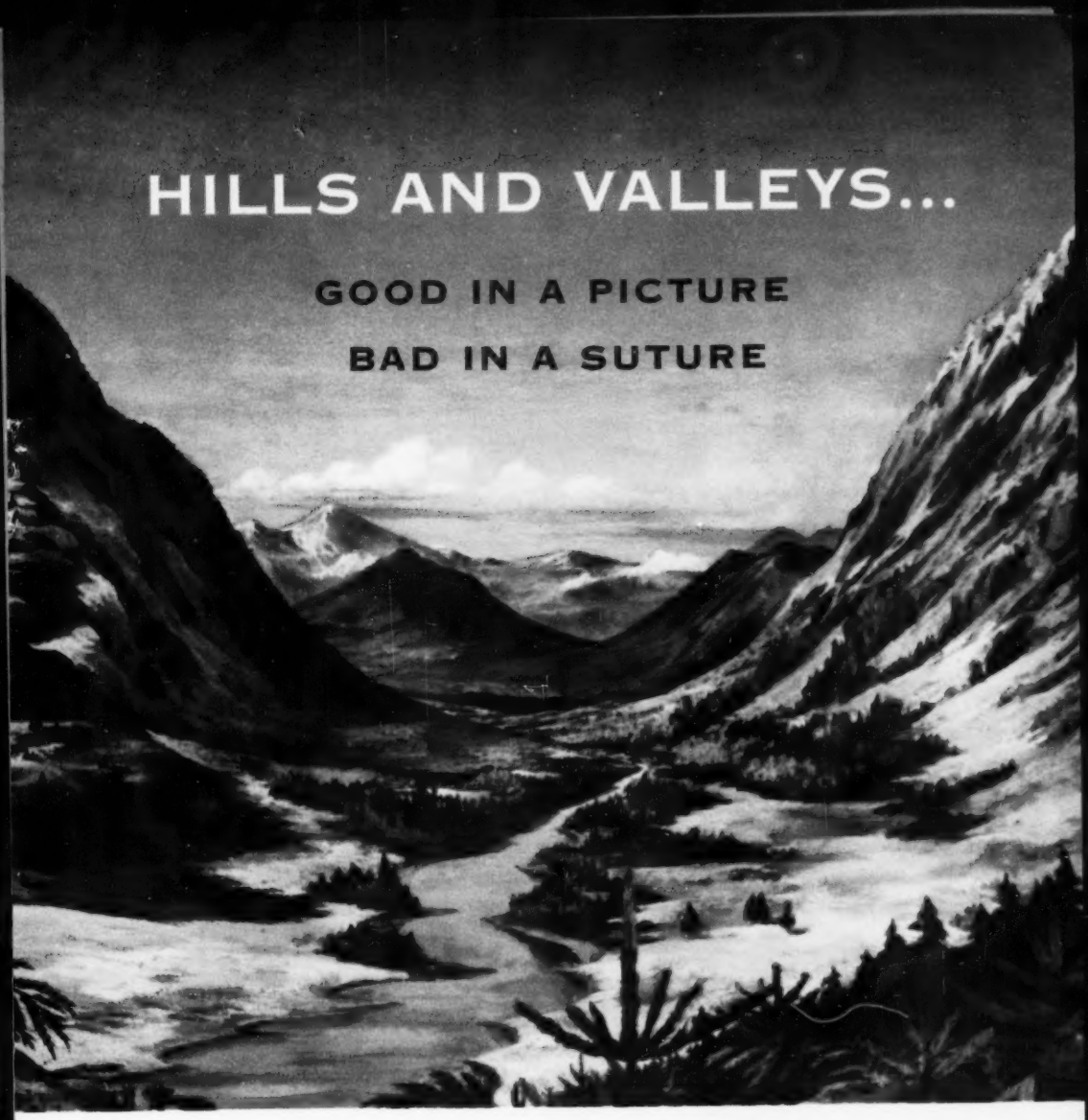


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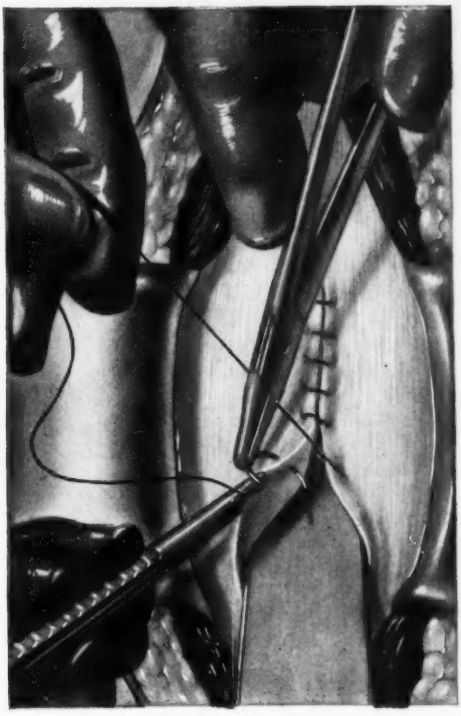

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# Editorials

## VARIATIONS IN MUCOSAL STRUCTURE OF STOMACH

### Their Implications in Operations for Resection of Gastric or Duodenal Ulcer

A RECENT survey of anatomical differences in stomachs observed at autopsy [1] has pointed to several facts which may pertain to the subject of gastric resection for duodenal ulcer.

These studies have shown that variations in stomach size, as measured by mucosal area, are more pronounced than differences in the external size of the stomach or of other organs. Moreover, the size of the stomach measured in this way cannot be correlated closely with body size. In 222 stomachs selected at random, the mucosal area varied between 421 and 1,536 sq. cm. These differences in mucosal area are not readily noticed unless the stomachs are distended or stretched to flatten the mucosal folds. In general, these folds are more prominent in a large empty stomach than in the average stomach with a smaller amount of mucosa. The large stomachs, therefore, tend to carry a larger quantity of mucosa per unit of external area. Because of this characteristic of the gastric mucosa, the surgeon may leave in the body a considerably larger amount of mucosa from a large stomach than he realizes because even the remaining relatively small area of contracted muscularis and serosa may cover a relatively large quantity of folded mucosa.

Unusually large stomachs occur without obstruction in cases of chronic duodenal ulcer; the latter, present in 30 cases of the above series, was never associated with a small stomach. In a radical gastric resection for duodenal ulcer, it would seem to be of particular importance, therefore, to reckon with the probability that the mucosal area to be dealt with will be considerably larger than average.

Measurements were also made of the two kinds of mucosa, antral and fundic. The antral portion is a comparatively small part of the total gastric mucosa; its area in the stomachs of patients with duodenal ulcer was usually between one-fifth and one-tenth of the total. Externally, however, this zone appeared relatively larger because mucosal folds are less conspicuous so that the surface of the mucosal area is more nearly equal to the external area of the contracted muscular wall in the antral portion than is the case in the rest of the stomach. Another important observation was the fact that the upper border of the antral mucosa extends higher on the lesser curvature than on the greater curvature, but that it lay at or below the middle of the lesser curvature in all but one of the measured cases of duodenal ulcer. In the one exceptional case there was severe chronic gastritis on the lesser curvature, and the upper border of the antral mucosa was obscured. Thus by high resection

From the Department of Pathology, Stanford University School of Medicine, San Francisco.

1. Cox, A. J., Jr.: A. M. A. Arch. Path. **54**:407 (Nov.) 1952.

on the lesser curvature in nearly all cases of duodenal ulcer complete proximal excision of the antrum should be readily achieved.

If it is of importance in planning operations also to remove a large part of the acid and pepsin-secreting tissue, our observation that the number of specific secretory cells is different in different portions of the fundic zone (body) of the mucosa assumes considerable interest. The greatest concentration of these cells was found in the distal portion of this zone, near the antrum, where in large stomachs the number of parietal cells per unit area of mucosa on the greater curvature was two to three times that encountered more proximally in the fundic zone; consequently, resection of the lower end of the fundic part of the stomach is most effective in reducing the number of secreting cells. In most large stomachs there are more secretory cells on the greater curvature than on the lesser by about 30% when the numbers are related to the mucosal area. The presence of more prominent mucosal folds on the greater curvature magnifies this difference between the borders of the stomach, so that a high line of resection on the greater curvature would be most likely to achieve the aim of a procedure designed to remove as large a part of acid-secreting tissue as possible.

Methods for measuring the amount of mucosal tissue in the stomach during life, and particularly an estimate of the mucosal area removed during operation, should be useful aids in planning gastrectomy procedures, and are clearly more desirable than other methods based on weight or on the measurement of the external surface alone. The need for specific information of this type in individual cases is somewhat lessened by the knowledge that a large stomach must be anticipated in cases of chronic duodenal ulcer and that the several anatomical features of large stomachs discussed above occur with good regularity. However, it is obvious that the mucosa is the secretory tissue and that anatomical variations in the mucosa of the stomach are therefore important in predicting the physiological effects of resective procedures. Unless the surgeon knows exactly what the kind of mucosa is and how much he removes, it will be difficult to predict the effect of the procedure on secretory activity.

ALVIN J. COX, M.D.

## THE POST-THROMBOTIC POSTSYMPATHECTOMY SYNDROME

CHRONIC ulceration of the lower extremity, secondary to a preexisting deep venous thrombosis, i. e., the so-called postphlebitic or post-thrombotic ulcer, has baffled the medical profession for centuries. Although not a fatal disease, it has resulted in an untold amount of human suffering and tremendous expense to the afflicted individuals, both in payment for unsuccessful therapy and, in addition, from the loss of wages due to disability. Numerous methods have been recommended to cure these ulcerations, but the vast majority have proved ineffective because they do not correct the underlying pathologic physiology.

A number of surgical procedures have been developed, which, although well-intentioned, are found unfortunately by further study to prove useless, or even detrimental. It is believed at present that lumbar sympathetic ganglionectomy in the treatment of the post-thrombotic type of ulceration of the lower extremity should be placed in this category. Experience has shown that when properly performed a sympathetic ganglionectomy is of great value in the treatment of various vascular disorders of the arteries, arterioles, and capillaries. This procedure has been

From the Surgical Department of the Massachusetts General Hospital, Boston.

recommended in recent years for the treatment of the post-thrombotic ulceration of the lower extremity because there appears to be slight hyperactivity of the sympathetic nervous system in a few of these limbs, as evidenced by hyperhidrosis and capillary stasis with cyanosis. This type of lesion, almost without exception, however, it is believed is not the result of arterial ischemia, but quite on the contrary develops because there is too much blood in the extremity. For this reason, since sympathetic ganglionectomy tends to increase the inflow of blood to a limb without aiding in its return, it would appear on careful analysis that this type of operative procedure could be detrimental to the extremity.

As a result of performing sympathetic ganglionectomies for the post-thrombotic type of ulceration of the lower extremity, it is believed a new disease entity has appeared. It is suggested that it be called the "post-thrombotic postsympathectomy syndrome," since it seems to develop only after this operative procedure has been performed for this type of lesion in the lower extremity. The condition is characterized by a chronic, indolent, painful ulceration involving frequently some portion of the dorsum of the foot or toes, whereas the original lesion is usually on the inner side of the lower leg or ankle. Because of its more distal location with frequent involvement of the toes, all attempts to heal it without complete bed rest and elevation of the extremity have proved unsuccessful. Furthermore, after it is healed by this means, it recurs almost as soon as the patient becomes ambulatory. In many instances the condition is far worse than the original simple post-thrombotic ulceration; in fact, it frequently approaches an incurable state. It becomes so incompatible with a normal existence, and interferes with a patient's livelihood, that in some instances a major amputation becomes the treatment of choice. All sympathectomized post-thrombotic extremities fortunately do not suffer to this extent, which if it were true would make the abandonment of this procedure for this disease relatively simple. However, it is believed that the few patients, if any, who may be benefited by sympathetic ganglionectomy for the post-thrombotic syndrome, with or without ulceration, are so far outweighed by the bad results that the procedure should be abandoned for all cases.

Evidence accumulating in regard to the etiology of the post-thrombotic ulceration indicates that it develops because of a state of ambulatory venous hypertension in the lower extremity, due to the incompetence of the "venous heart" in the lower limb from destruction of the venous valves in the deep veins by the preexisting venous thrombosis. This ulcerative lesion apparently develops because there is too much blood in the lower extremity at too high a pressure in the erect ambulatory state. This fact can be readily demonstrated by elevation of the limb above the level of the heart for a period of days to weeks with healing of the ulceration in practically all cases.

It is recommended, therefore, that the treatment of the postphlebitic syndrome, with or without ulceration, should attempt primarily to reestablish the function of the "venous heart" of the lower extremity to aid in the return of blood from it. This can best be performed by (1) elimination of the pooling of the blood in the enlarged subcutaneous venous reservoirs by a radical removal of the long and short saphenous veins with their tributaries, (2) by preventing regurgitation of blood into the deep veins in the erect position with interruption of either the superficial femoral or the popliteal vein, and (3) by attempting to control the lymphedema in the lower leg and to reestablish the function of the venous heart of the lower extremity through the use of an elastic support to the lower leg.

ROBERT R. LINTON, M.D.

# CLINICAL ANALYSIS OF BILLROTH I AND BILLROTH II SUBTOTAL GASTRIC RESECTIONS

HORACE G. MOORE JR., M.D.
RALPH J. SCHLOSSER, M.D.
JOHN K. STEVENSON, M.D.
HENRY N. HARKINS, M.D.
AND
HILDING H. OLSON, M.D.
SEATTLE

SUBTOTAL gastric resection is the most widely used operation for gastroduodenal ulceration. It is also used for certain lesions of the stomach requiring extirpative therapy, e. g., carcinoma, polyps, and leiomyomata. This paper will not be concerned with the relative merits of subtotal gastric resection versus other types of operation for these lesions. It behooves a surgeon from time to time to examine critically the results of that therapy which he believes to be best in order that he may modify it in any manner which would improve his results. This is the primary indication for this study.

Subtotal gastric resection as practiced today conforms to one of two general types, depending upon whether the duodenum or the jejunum is utilized for the reestablishment of gastrointestinal continuity. If the duodenum is utilized, the operation is known as a Billroth I; if the jejunum is employed, the procedure is a Billroth II, or one of its modifications.

In 1881 Billroth[1] performed the first successful resection of a portion of the stomach, with reestablishment of continuity by gastroduodenostomy. This procedure was performed in 1879 by Péan[2] and in 1880 by Rydygier,[3] but in both cases the patients died.

---

From the Division of Surgery, King County Hospital, and the Department of Surgery, University of Washington School of Medicine.

This work was aided by Grants from the National Institutes of Health (Project G-3479) and Initiative 171 Research Funds of the State of Washington.

Read before the Section on Surgery, General and Abdominal, at the One Hundred and First Annual Session of the American Medical Association, June 12, 1952.

1. Billroth, T.: Offenes Schreiben an Herrn L. Wittelshöfer, Wien. med. Wchnschr. **31**: 161-165, 1881; cited by Bruusgaard, C.: The Operative Treatment of Gastric and Duodenal Ulcer: Clinical and Roentgenologic Study, Acta chir. scandinav. (Supp. 117) **94**:1-435, 1946.

2. Péan, J. E.: De l'ablation des tumeurs de l'estomac par la gastrectomie, Gaz. hôp., Paris **52**:473-475, 1879; cited by W. J. Mayo: Radical Operations on the Stomach with Especial Reference to Mobilization of the Lesser Curvature, Surg., Gynec. & Obst. **36**:447-453 (April) 1923.

3. Rydygier, L.: Über Magen-Resection mit Demonstration von Praeparaten, Arch. klin. Chir. **26**:731-743, 1881; cited by W. J. Mayo: Radical Operations on the Stomach with Especial Reference to Mobilization of the Lesser Curvature, Surg., Gynec. & Obst. **36**:447-453 (April) 1923.

The Billroth II operation was not developed to overcome the difficulties of the Billroth I method. Initially, Billroth planned a two-stage procedure because of the debility of a patient who was to undergo partial gastric resection. The first stage was to be an anterior gastrojejunostomy, to be followed by a pylorectomy as the second stage. However, the patient withstood the operative procedure well, and the two stages were completed at one time. Thus, a new operation, known as the Billroth II, was created in the year 1885.[4]

Mainly because of the frequent leakage at the so-called critical angle, i. e., the angle formed by the anastomotic suture line of the gastroduodenostomy and the suture line necessary to decrease the circumference of the stomach, the Billroth I procedure became unpopular shortly after its inception.[5] This prejudice of the last century has been carried forward to the present and has contributed to the more widespread use of the Billroth II operation and its modifications over the Billroth I operation when subtotal gastric resection is used.

However, in recent years certain advantages of the Billroth I procedure have been described by some authors,[6] and, consequently, its popularity is increasing.

The specific purposes of this study are threefold: (1) a clinical analysis of subtotal gastric resection as carried out in a county hospital, (2) a comparison of a Billroth I and a Billroth II series in the same hospital for the same time period from the standpoint of technical feasibility of performance and results, and (3) a comparison of the entire series with the mortality, recurrence, and postoperative satisfaction in similar series elsewhere.

## MATERIAL

The material for this study includes all gastric resections, except total gastrectomies, performed in the King County Hospital from Jan. 1, 1948, through March 31, 1952, regardless of the pathology for which the resections were performed.

There are two main factors which determined whether the reestablishment of continuity would be according to the Billroth I or the Billroth II technique in this series. First, the decision depended on the particular preference of the surgeon who performed the operation. Many of the Billroth II operations might have been done as Billroth I procedures if the operating surgeons had so preferred. Eleven different surgeons performed the entire series

4. von Hacker: Zur Kasuistik und Statistik der Magenresektionen und Gastroenterostomien, Arch. klin. Chir. **32**:616-625, 1885; cited by Spivack, J. L.: The Surgical Technic of Abdominal Operations, Ed. 2, Chicago, S. B. Debour Publishers, 1938.

5. Mayo, W. J.: Radical Operations on the Stomach with Special Reference to Mobilization of the Lesser Curvature, Surg., Gynec. & Obst. **36**:447-453 (April) 1923.

6. (*a*) Clagett, O. T., and Waugh, J. M.: Indications for and Advantages of Schoemaker-Billroth I Gastric Resection, Arch. Surg. **56**:758-765 (June) 1948. (*b*) Higginson, J. F., and Clagett, O. T.: Gastric Resection: The Schoemaker-Billroth I Operation, Surgery **24**:613-620 (Oct.) 1948. (*c*) Fallis, L. S., and Barron, J.: Von Haberer-Finney Gastrectomy with Vagotomy, Arch. Surg. **59**:758-767 (Sept.) 1949. (*d*) Balfour, D. C.: The Status of the "Billroth No. I" in the Surgery of Stomach and Duodenum, Surg., Gynec. & Obst. **58**:917-919 (May) 1934. (*e*) Perman, E.: The So-Called Dumping Syndrome After Gastrectomy, Acta med. scandinav., Supp. 196, pp. 361-365, 1947. (*f*) Bohmansson, G.: On the Technique of Partial Gastrectomy (Billroth I), Acta chir. scandinav. **75**:221-241, 1934. (*g*) Moore, H. G., Jr., and Harkins, H. N.: Experiences with the Billroth I Subtotal Gastric Resection, West. J. Surg. **60**:264-275 (June) 1952. (*h*) Moore, H. G., Jr., and Harkins, H. N.: A Critical Evaluation of the Billroth I Gastric Resection, Surgery **32**:408-425 (Aug.) 1952.

of Billroth I operations. We had a preference for the Billroth I operation, and, consequently, in this series 85.5% of the operations were performed in our service. The Billroth II series of operations were performed by 36 different surgeons.

The second factor in determining whether each operation would fall into the Billroth I or the Billroth II series was whether it came early or late in the series. As our technical experience with the Billroth I operation increased, we found that we were able to utilize this procedure in many cases in which we would previously have used the Billroth II procedure. The realization that we could broaden the scope of the Billroth I operation by using the von Haberer-Finney end-to-side modification has contributed to the late rise in frequency of the Billroth I technique over the Billroth II (Fig. 1). We have performed the von Haberer-Finney end-to-side modi-

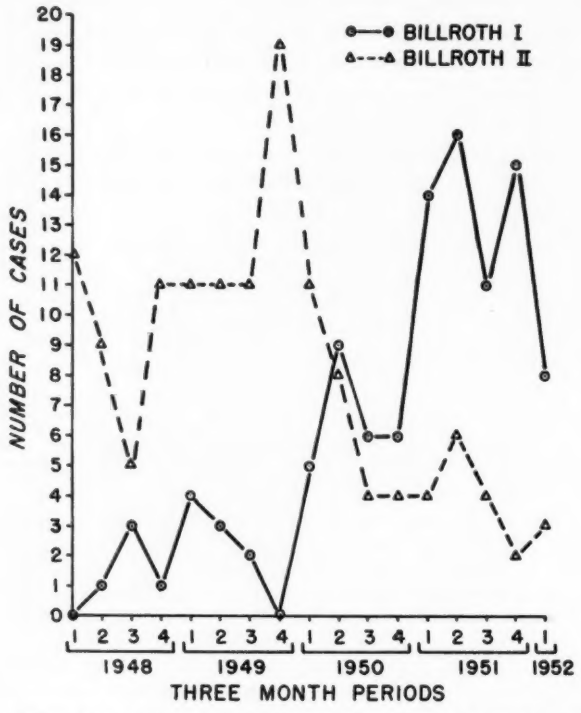


Fig. 1.—Comparison of the frequency of performance of the Billroth I and Billroth II procedures, by three-month intervals (Jan. 1, 1948, to March 31, 1952) in the King County Hospital series.

fication seven times in the series; only two of these operations were done in this series prior to October, 1951, the others having been done in the last five and one-half months of the series. Fallis and Barron [6c] have stressed the usefulness of this modification.

The follow-up data in this series were obtained, with few exceptions, by personal interview by one of us. Several of the patients were contacted by telephone. In general, the completeness of the follow-up is better in the Billroth I series than in the Billroth II series. This is because in the majority of the cases in the former group the operation was performed more recently, and better rapport was established early with these patients. The follow-up in the entire series is poorer than one might find in a series drawn from private practice, because many of our patients are transients and alcoholics and cannot be depended upon to keep follow-up appointments.

ANALYSIS OF MATERIAL

The material consists of 104 Billroth I and 135 Billroth II operations.

*Age.*—The age incidence for both series is shown in Figure 2. In the Billroth I series the youngest patient was 22 years old, and the oldest was 83. In the Billroth II series the extremes were 25 and 89 years. The average age of patients in the Billroth I series was 57 years and in the Billroth II series, 58 years.

*Sex.*—Table 1 shows the proportion of men and women in the two series, with men predominating in each group.

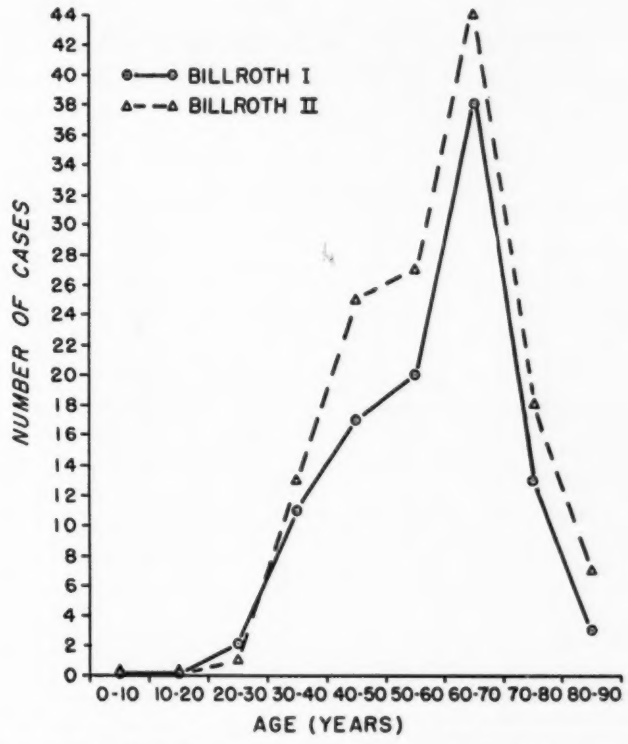


Fig. 2.—Age incidence of patients in the Billroth I and Billroth II series. Shape of the curve is the same in the two series. Largest incidence for any decade occurred in patients in the 60- to 70-year age bracket.

*Duration of History.*—The average duration and ranges of duration of history are shown in Table 2 and are similar for the Billroth I and the Billroth II series.

*Frequency of Indications.*—Table 3 is a tabulation of the frequency with which various indications for operation are observed in the two series. In many of the cases more than one of the indications are tabulated. Bleeding is the most frequent indication seen in the two series. The high incidence of alcoholism also is to be noted; most probably this is an indication peculiar to a county hospital type of practice. In general, because of the unreliability of most of our patients, we advise

resection at the time of acute perforation of an ulcer if the perforation is early and the patient's general condition permits. There were four such cases in each series recognized preoperatively and another in the Billroth I group not recognized until the time of operation.

*Pathology.*—Reference is made to Figures 3 and 4 and Table 4. In the majority of the cases in both series the patients had peptic ulcer. In the Billroth I series, 70.4% of the ulcer patients had duodenal pathology. In the Billroth II series,

TABLE 1.—*Sex Incidence*

| | Billroth I | | Billroth II | |
|---|---|---|---|---|
| Sex | No. Patients | Per Cent | No. Patients | Per Cent |
| Male | 79 | 76.0 | 113 | 83.7 |
| Female | 25 | 24.0 | 22 | 16.3 |
| Total | 104 | 100 | 135 | 100 |

TABLE 2.—*Duration of History*

| | Billroth I | Billroth II |
|---|---|---|
| No. of cases known | 90 | 125 |
| Average duration, yr. | 6.7 | 7.9 |
| Range, yr. | 0-30 | 0-30 |

TABLE 3.—*Frequency of Indications for Surgery*

| | Billroth I | | Billroth II | |
|---|---|---|---|---|
| | No. Times Present | Cases with Indication, % | No. Times Present | Cases with Indication, % |
| Bleeding | 46 | 44.2 | 85 | 62.9 |
| Intractibility | 36 | 34.6 | 22 | 16.3 |
| Gastric ulcer | 35 | 33.7 | 14 | 10.4 |
| Previous perforations | 25 | 24.0 | 25 | 18.5 |
| Obstruction | 23 | 22.1 | 20* | 14.8* |
| Alcoholism | 11 | 10.6 | 28 | 20.7 |
| Carcinoma | 10 | 9.6 | 3 | 2.2 |
| Acute perforation present | 4 | 3.8 | 4 | 3.0 |
| Gastric polypi | 2 | 1.9 | 0 | 0 |
| Hypertrophy of pylorus | 1 | 1.0 | 0 | 0 |
| Increasing obesity with ulcer diet | 1 | 1.0 | 0 | 0 |
| Stomal ulcer (previous inadequate resection) | 1 | 1.0 | 3 | 2.2 |
| Stomal ulcer (previous gastroenterostomy) | 1 | 1.0 | 4 | 3.0 |
| Esophageal stricture and hiatal hernia | 0 | 0 | 1 | 0.7 |
| Recurrent duodenal ulcer after Finney pyloroplasty | 0 | 0 | 1 | 0.7 |

* One previous Billroth I operation done elsewhere.

82.0% of the ulcer patients had duodenal pathology. It is of interest that in the Billroth II group there were three cases in which a previous gastroenterostomy was done, with active duodenal ulcer at the time of resection. Figure 3 indicates the increasing incidence of Billroth I operations in the group with duodenal pathology.

*Extent of Resection.*—We have recently become interested in measuring the extent of resection and feel that it is most difficult to evaluate any extirpative operation for peptic ulcer unless objective data are available on the extent of resec-

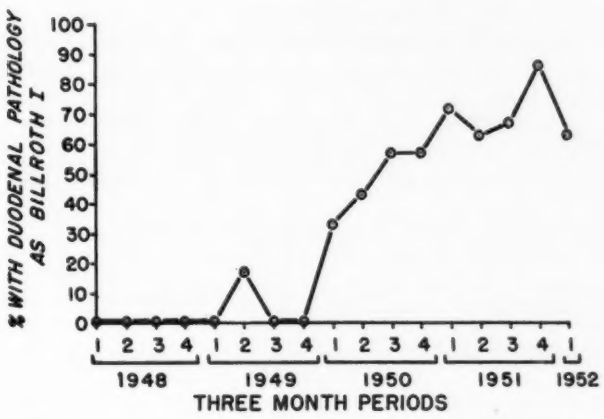


Fig. 3.—Per cent of total cases with duodenal ulcer pathology in which Billroth I operation was carried out.

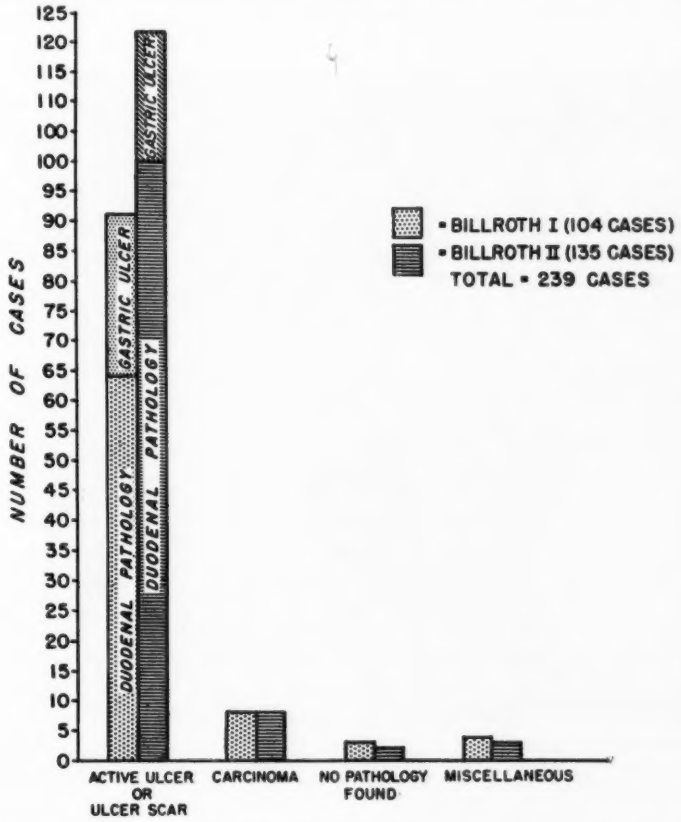


Fig. 4.—Bar graph representation of pathology in cases in which subtotal resection was carried out. Pathology report is given in greater detail in Table 4.

TABLE 4.—*Pathology*

| Pathology | Billroth I | | Billroth II | |
|---|---|---|---|---|
| | No. Cases | % of Ulcer Cases | No. Cases | % of Ulcer Cases |
| Active ulcer or ulcer scar | 91 | 100 | 122 | 100 |
| Gastric | 27 | 29.6 | 22 | 18.0 |
| Duodenal | 50 | 55.0 | 88* | 72.2* |
| Acute perforation | 5 | .... | 4 | .... |
| Mixed (gastric and duodenal and stomal) | 12 | 13.2 | 12 | 9.8 |
| Healed duodenal ulcer and carcinoma of stomach present | 2 | 2.2 | 0 | 0 |
| Incidence of ulcer cases with duodenal pathology | 64 | 70.4 | 100 | 82.0 |
| Carcinoma | 6 | .... | 8 | .... |
| Hypertrophy of pylorus | 2 | .... | 0 | .... |
| Associated with hiatus hernia, inflammation lower esophagus | 1 | .... | .. | .... |
| Gastric polypi and leiomyomata | 1 | .... | 0 | .... |
| Postgastritic pseudopolypi | 1 | .... | 0 | .... |
| No pathology found | 3 | .... | 2 | .... |
| Lymphosarcoma | 0 | .... | 1 | .... |
| Angulation of old gastrojejunostomy | 0 | .... | 1 | .... |
| Esophageal stricture and hiatal hernia | 0 | .... | 1 | .... |
| Total | 104 | | 135 | |

* One patient had leiomyoma of stomach associated with duodenal ulcer.

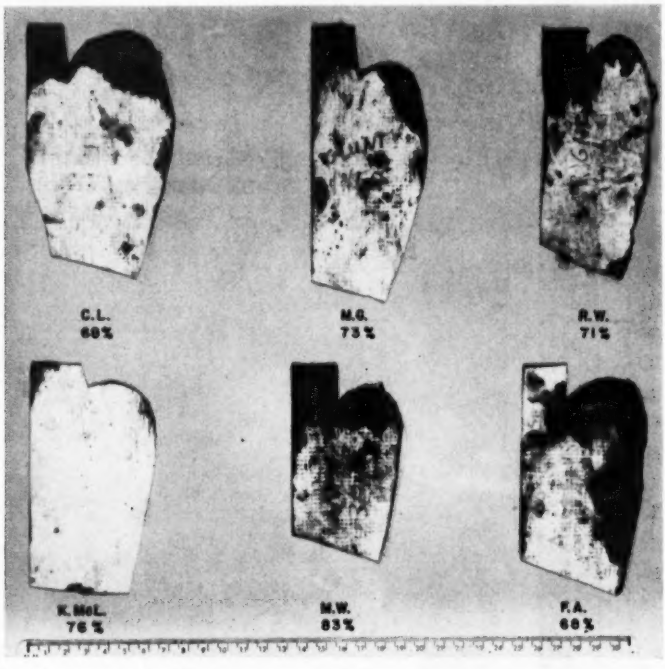


Fig. 5.—Photograph showing some actual patterns of residual stomach segment from six representative Billroth I subtotal gastric resections, with amounts resected as measured by the polar planimeter. Patient's initials and per cent of resection are given below the respective patterns.

tion. We have recently submitted a paper for publication [6h] in which we described a new method for determining extent of resection by measuring the areas of patterns of the residual stomach and the actual stomach removed, the two measurements being made with the polar planimeter. Figure 5 is a photograph of some of the cottonoid patterns of residual stomachs made at the time of surgery. Unfortunately, we have no data on extent of resection in the Billroth II series. Table 5 shows the average values obtained in the Billroth I series for the four criteria used: curvature

TABLE 5.—*Extent of Resection (Average Values)*

| Curvature Measurements | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Lesser | | Greater | | Weight | | Surgeon's Estimate | | Planimeter | |
| No. Measured | Cm. | No. Measured | Cm. | No. Measured | Gm. | No. Estimated | Per Cent | No. Measured | Per Cent |
| 86 | 14 | 86 | 23 | 88 | 210 | 70 | 71 | 32 | 72 |

TABLE 6.—*Postoperative Complications*

| Complication | Billroth I | | Billroth II | |
|---|---|---|---|---|
| | No. Times Present | Cases with Complication, % | No. Times Present | Cases with Complication, % |
| Atelectasis and/or bronchopneumonia | 11 | 10.6 | 7 | 5.2 |
| Hospital deaths | 4 | 3.8 | 10 | 7.4 |
| Wound infection | 2 | 1.9 | 14 | 10.4 |
| Mechanical intestinal obstruction | 2 | 1.9 | 3 | 2.2 |
| Extreme adynamic ileus | 2 | 1.9 | 0 | 0 |
| Postoperative bleeding (gastrointestinal) | 1 (mild) | 1.0 | 3 (1 death) | 2.2 |
| Urinary tract infection | 1 | 1.0 | 0 | 0 |
| Cerebrovascular accident or myocardial infarct | 1 | 1.0 | 4 | 3.0 |
| Epidydimitis | 1 | 1.0 | 1 | 0.7 |
| Early stomal edema (spontaneously relieved) | 1 | 1.0 | 0 | 0 |
| Transfusion reaction | 1 | 1.0 | 0 | 0 |
| Pulmonary embolus | 0 | 0 | 4 | 3.0 |
| Thrombophlebitis | 0 | 0 | 3 | 2.2 |
| Suture-line leakage | ?1 * | ?1.0 * | 2 | 1.5 |
| Wound dehiscence | 0 | 0 | 1 | 0.7 |
| Incisional hematoma | 0 | 0 | 1 | 0.7 |
| Subhepatic abscess | 1 | 1.0 | 1 | 0.7 |
| Pancreatitis | 0 | 0 | 1 | 0.7 |
| Liver necrosis | 0 | 0 | 1 | 0.7 |

* Patient had subhepatic abscess at autopsy; no mention of suture-line leakage.

measurements, weight, surgeon's estimate, and planimeter measurement. These values include gastric as well as duodenal pathology.

*Distance of Major Papilla from Severed End of Duodenum.*—In 24 of the Billroth I cases, we measured the distance between the entrance of the common bile duct at the major papilla to the severed end of the duodenum. It is of interest that the papilla can be felt most easily from the left side of the table, using the left index finger in the open duodenal stump. The average distance was 5.8 cm., ranging between 2.0 and 8.0 cm. A von Haberer-Finney anastomosis was performed in five of these cases, and the average distance measured was 4.4 cm., with a range of 2.0 to 6.5 cm. Unfortunately, we have no similar data for the cases in the Billroth II series.

*Postoperative Complications.*—The complications in the immediate postoperative period are recorded in Table 6. Pulmonary complications and wound infection were the ones most commonly encountered. The hospital mortality rate for the entire Billroth I group is 3.8% and for the Billroth II series, 7.4%.

TABLE 7.—*Poor-Result Cases (Includes Operative Deaths)*

| Case | Type of Operation | Description |
|---|---|---|
| 1 | Billroth I | 77-yr.-old white woman with bleeding gastric ulcer; died 21 days postoperatively with a myocardial infarct and bronchopneumonia |
| 2 | Billroth I | 80-yr.-old white woman with carcinoma of stomach; died 5 wk. postoperatively with pulmonary embolism and subphrenic abscess; no information as to whether or not there was suture-line leakage |
| 3 | Billroth I | 69-yr.-old white woman with carcinoma of stomach; died 11 mo. postoperatively of persistence of carcinoma |
| 4 | Billroth I | 70-yr.-old white man with pyloric hypertrophy and inflammatory stricture of lower esophagus; 25% of lower stomach resected and also esophageal segmental resection; died 44 hr. postoperatively; autopsy not granted |
| 5 | Billroth I | 67-yr.-old white man with bleeding gastric ulcer and duodenal scar; postoperative paralytic ileus; reexploration 9 days postoperatively; wound dehiscence and enteric fistula developed after second operation; died 28 days after Billroth I procedure |
| 6 | Billroth I | 73-yr.-old white man with benign prepyloric ulcer; minimal resection 2 in. on each side of ulcer; 3 mo. later stomal obstruction developed with inflammatory reaction and gastrojejunostomy was done |
| 7 | Billroth II | 57-yr.-old white man with duodenal ulcer; died 3 days postoperatively of pulmonary embolus |
| 8 | Billroth II | 73-yr.-old white woman with gastric ulcer; died 11 days postoperatively of coronary thrombosis |
| 9 | Billroth II | 65-yr.-old white woman with gastric ulcers; died 14 days postoperatively of duodenal stump leakage |
| 10 | Billroth II | 46-yr.-old white man with bleeding duodenal ulcer; died 8 days postoperatively of gastrointestinal hemorrhage, source undetermined; suture line intact at necropsy |
| 11 | Billroth II | 66-yr.-old white woman with bleeding duodenal ulcer; died 1 day postoperatively of suture-line leakage |
| 12 | Billroth II | 57-yr.-old white man with bleeding gastric ulcer; died in operating room |
| 13 | Billroth II | 86-yr.-old white man with bleeding duodenal ulcer; died 41 days postoperatively of coronary occlusion |
| 14 | Billroth II | 89-yr.-old white woman with obstructed gastrojejunostomy; died 2 days postoperatively because of technical error of severing common duct and hepatic artery |
| 15 | Billroth II | 84-yr.-old white man with obstructed duodenal ulcer; died 7 days postoperatively of atelectasis |
| 16 | Billroth II | 58-yr.-old white man with gastric ulcer; died less than 1 day postoperatively; cause unknown |
| 17 | Billroth II | 59-yr.-old white man with carcinoma of stomach; palliative resection; died 3 mo. postoperatively of carcinomatosis |
| 18 | Billroth II | 75-yr.-old Japanese man with carcinoma of stomach; died 28 mo. postoperatively of persistent carcinoma |
| 19 | Billroth II | 38-yr.-old Negro man with stomal ulcer; bleeding stomal ulcer developed necessitating emergency operation |
| 20 | Billroth II | 44-yr.-old white woman with acute perforation of duodenal ulcer; gastrojejunocolic fistula developed 3 mo. postoperatively |
| 21 | Billroth II | 60-yr.-old white man with duodenal ulcer; severe dumping and marginal ulcer necessitating vagotomy 6 mo. later |
| 22 | Billroth II | 67-yr.-old white man with duodenal ulcer; symptoms of possible marginal ulcer 3 yr. postoperatively |
| 23 | Billroth II | 62-yr.-old white man with duodenal ulcer; symptoms of possible marginal ulcer developed about 6 mo. postoperatively |
| 24 | Billroth II | 66-yr.-old white man with duodenal ulcer; stomal obstruction developed necessitating reexploration |
| 25 | Billroth II | 47-yr.-old white man with gastric ulcer; has severe dumping 10 mo. postoperatively |

There was one patient with early stomal edema (spontaneously relieved) in the Billroth I group, but this condition was not present in any of the Billroth II patients.

There were two instances of suture-line leakage in the Billroth II group and one possible instance in the Billroth I series, although we have insufficient autopsy information to be certain.

There were five patients in the combined series with myocardial infarcts or cerebrovascular accidents, a reflection of the high incidence of elderly patients.

*Follow-Up Studies.*—Postoperatively these patients were followed for periods up to 52 months. We have some follow-up data on 92, or 88.5%, of the Billroth I patients and on 76, or 56.2%, of the Billroth II patients. We have classified the results in follow-up cases into three categories, according to the degree of postoperative satisfaction: 1. Excellent. A patient must have no evidence, subjectively or objectively, of any disability or postgastrectomy syndrome limiting desired activity of that patient. 2. Satisfactory. These patients may have minor postgastrectomy syndromes, such as occasional diarrhea, mild dumping, etc., which are not severe enough to prevent average activity. 3. Poor. This group includes all hospital deaths, those with recurrent ulcer, anastomotic leakage, stomal obstruction, and those who exhibit disability which interferes with average activity.

It is to be emphasized that this classification is based on information obtained at the time when the patient was last seen in the follow-up and that many of these patients may fall into different categories in the future when a longer follow-up is available.

A brief description of the cases in which the results were considered poor is contained in Table 7. There are six such cases in the Billroth I group, or 6.5% of those followed. This includes four hospital deaths, with a hospital mortality rate

TABLE 8.—*Postoperative Weight Change*

| | Weight | | | | | |
|---|---|---|---|---|---|---|
| | Loss | | Same | | Gain | |
| Type of Operation | No. of Cases | Per Cent | No. of Cases | Per Cent | No. of Cases | Per Cent |
| Billroth I, 74 cases followed | 19 | 25.7 | 21 | 28.3 | 34 | 46.0 |
| Billroth II, 45 cases followed | 21 | 46.6 | 12 | 26.7 | 12 | 26.7 |

of 3.8%. There are 19 poor-result cases in the Billroth II group, with 10 hospital deaths (hospital mortality rate of 7.4%).

Most reported series consider only mortality following gastric resection for peptic ulcer and do not include cases of carcinoma and of esophageal stricure. If this custom is followed, our mortality in peptic ulcer cases was 2.2% in 91 Billroth I cases and 8.2% in 122 Billroth II cases.

There was one patient in the Billroth I group in whom stomal obstruction developed which necessitated reoperation and one who had early stomal obstruction due to edema which was spontaneously relieved. One patient in the Billroth II group had stenosis of the stoma and required another operation.

Only one Billroth I patient had possible suture-line leakage (information is insufficient to establish this with certainty), while there were two such instances in the Billroth II series.

Of those patients followed in the Billroth I group, none have had recurrent ulcers. In the Billroth II series there are three patients with recurrent ulcers, as determined by follow-up, and two other patients in this group with symptoms of marginal ulcer, but these are not proved recurrences.

We have obtained data on postoperative changes in body weight from the weight at the time of operation in 74 of the Billroth I cases and in 45 of the Billroth II cases (Table 8). In the former, 74.3% of patients either maintained or surpassed their operative weight. In the Billroth II group, only 53.4% of patients either maintained or surpassed their operative weight.

It has been possible to follow 79 of the Billroth I patients and 61 of the Billroth II patients for the dumping syndrome. We have chosen the following definition of the dumping syndrome: the occurrence of nausea, sweating, palpitation, and/or subjective flushing or explosive diarrhea, during or immediately after the ingestion of food, relieved by recumbency. It is to be emphasized that these symptoms may occur to a mild degree and cause the patient little or no disability and may be associated only with overeating in certain cases. These criteria, as we use them, are justifiably strict because it is important to detect the qualitative presence of

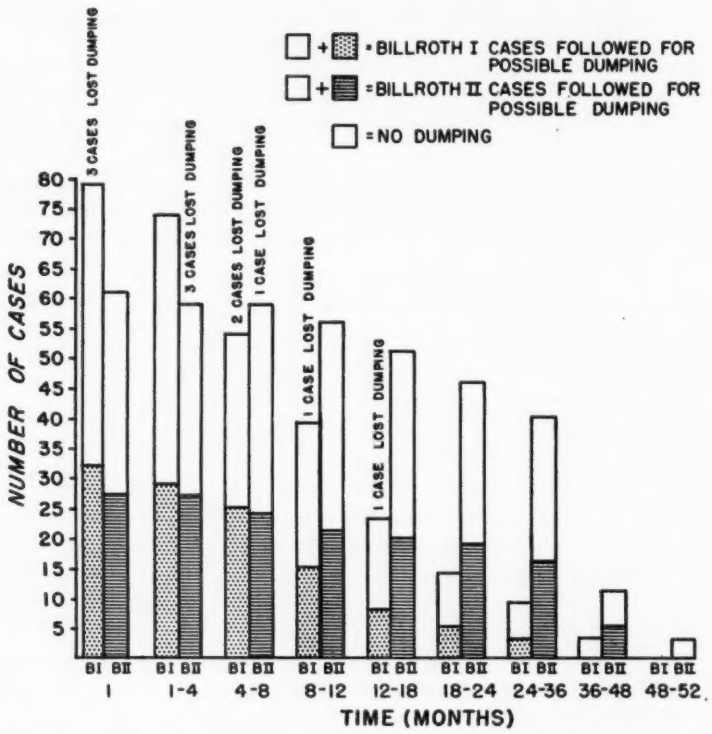


Fig. 6.—Cumulative representation of dumping syndrome in the two series of cases with subtotal gastric resection for the time periods designated. Total height of the columns represnets cases with follow-up for possible dumping. Shaded portion of columns represents cases in which dumping occurred. Also designated are those cases in which dumping occurred and later disappeared during the indicated time interval.

whatever mechanism is responsible for the dumping syndrome, regardless of severity, if we are ever to elucidate the pathologic physiology of "dumping."

In all of our patients with dumping, the symptoms have developed within the first two postoperative weeks. In some patients the dumping syndrome disappeared entirely, while others had less severe symptoms with the passage of time.

According to the present follow-up, none of the Billroth I patients have severe dumping. Only two of the Billroth II patients have severe dumping. With use of the strict criteria, 40.5% of the Billroth I and 44.3% of the Billroth II patients had

symptoms of dumping. Six of the Billroth I group and four of the Billroth II group lost all evidence of dumping during the period followed, leaving 32.9% in the Billroth I series and 37.7% in the Billroth II series with persistent dumping for the periods followed (Fig. 6).

Table 9 categorizes the patients followed in both series according to over-all evaluation of results of operation at the longest time followed. There are 93.5% of the Billroth I group in whom the results are considered satisfactory or excellent, while 75.0% of the Billroth II patients fall into these two groups.

## COMMENT

Wangensteen [7] has stressed the importance of extent of resection in the evaluation of recurrent ulceration after subtotal gastric resection for peptic ulcer. He has shown that one may expect anacidity after 75% resection. At the Mayo Clinic, in Rochester, Minn., a method of estimating extent of resection is used which is based on an empirical relation between the thickness of the muscularis and the

TABLE 9.—*Results*

| | Poor | | Satisfactory | | Excellent | |
|---|---|---|---|---|---|---|
| Time, Mo. | Billroth I | Billroth II | Billroth I | Billroth II | Billroth I | Billroth II |
| 1 | 3 | 9 | 2 | .. | 3 | 2 |
| 1- 4 | 2 | 4 | 15 | .. | 9 | .. |
| 4- 8 | .. | 1 | 11 | .. | 6 | 3 |
| 8-12 | 1 | 1 | 9 | 1 | 7 | 2 |
| 12-18 | .. | .. | 6 | 1 | 4 | 4 |
| 18-24 | .. | 2 | 3 | 2 | 2 | 4 |
| 24-36 | .. | 1 | 2 | 12 | 3 | 16 |
| 36-48 | .. | 1 | 3 | 4 | 1 | 3 |
| 48-52 | .. | .. | .. | .. | .. | 3 |
| Total no. of cases | 6 | 19 | 51 | 20 | 35 | 37 |
| Total percentage of cases followed | 6.5 | 25.0 | 55.5 | 26.4 | 38.0 | 48.6 |

weight of the resected specimen.[8] We believe that the planimeter method of measuring patterns of residual and resected stomach, described in a previous publication,[6h] is a reliable measurement of extent of resection. We have had the opportunity to take a pattern measurement at autopsy of the residual stomach of a Billroth I patient who was operated upon and who died since the termination of the present series. The pattern taken at the time of surgery measured 50.0 sq. cm., and the pattern at autopsy had an area of 57.5 sq. cm. This variation causes a difference of only 2% between the value for per cent resected obtained at the operation and that of the autopsy. It is well for the surgeon to calibrate his estimation of extent of resection by some such objective method in order that he may be more nearly certain of achieving the goal for which the resection is undertaken.

One of the criticisms often made of the Billroth I resection is that only a limited resection can be performed when the duodenum is utilized for anastomosis.[9] In 32 of our cases in which measurements were made with the planimeter, we have

7. Wangensteen, O. H.; Varco, R. L.; Hay, L.; Walpole, S., and Trach, B.: Gastric Acidity Before and After Operative Procedure with Special Reference to the Role of the Pylorus and Antrum, Ann. Surg. **112**:626-667 (Oct.) 1940.

8. Dockerty, M. B.: Personal communication to the authors.

9. Footnote 6 *a-d*.

resected an average of 72% of the stomach (Table 5). Thus, on the basis of our own experience, we feel that this criticism is not justified.

Unfortunately, such data are not available for our Billroth II series.

Many surgeons agree that the Billroth I procedure can be performed on most patients with gastric pathology, but few admit its feasibility on patients with duodenal pathology. We believe that there are, indeed, few cases of duodenal ulcer in which the Billroth I procedure cannot be used (Fig. 3). Duodenal pathology was present in 70.4% of our Billroth I cases and in 82.0% of the Billroth II series. There has not been a Billroth II operation performed in our service for seven months. This is largely due to the fact that we have utilized the von Haberer-Finney end-to-side modification of the Billroth I procedure since that time in those cases in which it is necessary to leave the ulcer or ulcer scar in the duodenum. In most of these cases the typical end-to-end anastomosis is unsuitable. We have found it very helpful in these cases to divide the duodenum according to the Strauss method,[10] which we have illustrated elsewhere.[6h]

Extensive mobilization of the duodenum does not interfere with the common bile duct, as feared by some. Actually the major papilla is more distal in the duodenum than is commonly realized. The average distance of the major papilla from the severed end of the duodenum was 5.8 cm. in 24 cases in which it was measured.

The hospital mortality rate for the Billroth I series is 3.8%. All patients who died in the hospital were over 67 years of age, and these tabulations are shown in Table 7. In the Billroth II series the hospital mortality rate was 7.4%, almost twice that of the Billroth I group. These patients ranged from 57 to 89 years of age. If only peptic ulcer cases are considered the mortality rates are 2.2% (Billroth I) and 8.2% (Billroth II). In 1947 Morley [11] reported 346 cases of gastric ulcer, with resection performed according to the Billroth I method, with a mortality rate of 4.3%. In 72 cases with resection for duodenal ulcer the mortality rate was 2.8%. Maingot [12] stated that the mortality of patients with the Billroth II subtotal resection for duodenal ulcer should no greater than 1 or 3%. Gray and Williams [13] reported 223 duodenal ulcer cases with Billroth II resection and with a mortality of 4.9%. Eastman and Cole [14] stated that the death rate in cases of subtotal gastrectomy for benign ulcer should be less than 3%. They reported a series of subtotal gastrectomies for carcinoma with a mortality rate of 11.4%.

Thus, when compared with the experiences of others, our Billroth I hospital mortality rate is probably acceptable, particularly considering the high age incidence of our patients. The hospital death rate for our Billroth II patients is somewhat high.

There is no known instance of recurrent ulceration in the Billroth I group. In the follow-up of the Billroth II group, excluding hospital deaths, there are three known instances (4.5%) of recurrent ulceration and two other possible cases,

10. Strauss, A. A.: Personal communication to the authors.

11. Morley, J., cited by Maingot, R.: Abdominal Operations, New York, Appleton-Century-Crofts, Inc., 1948.

12. Maingot, R.: Abdominal Operations, New York, Appleton-Century-Crofts, Inc., 1948.

13. Gray, H. K., and Williams, R. R., Jr.: Results of Classic Operations for Duodenal Ulcer: 5 to 10 Year Follow-Up in 532 Cases, J. A. M. A. **141**:509-513 (Oct. 22) 1949.

14. Eastman, W. H., and Cole, W. H.: Precautions and Results in Gastrectomy, Arch Surg. **59**:768-782 (Sept.) 1949.

making a total of five possible recurrences (7.6%). Wangensteen and his associates[15] have observed a recurrence rate of 1.1% in their Billroth II series. Our recurrence rate with the Billroth II procedure is too high to be acceptable. It is only fair to the Billroth II procedure per se to point out, before comparing our Billroth I and Billroth II recurrence rates, that (1) the Billroth II cases had so few quantitative measurements of extent of resection that the possibility that they represent less radical resections is to be entertained and that (2) a higher percentage of cases in the Billroth II series was done in other services than in our own (53.1% as compared with 14.5% for the Billroth I series).

In our series the cases followed for dumping in the Billroth I and Billroth II groups have an incidence of this syndrome of 40.5% and 44.3%, respectively. It is to be emphasized again that these figures are based on the strict criteria outlined in the section of our report entitled Analysis of Material. Only two patients in the entire series are considered to have severe dumping, and both of them are in the Billroth II group. There are reports of dumping incidence in the literature varying from 0 to 75%.[16] Undoubtedly, part of this discrepancy is based on variation in strictness of criteria. Perman [6e] found a lower incidence in the Billroth I group than in the Billroth II group. Baker,[17] speaking of the Billroth I procedure in comparison with the Billroth II, stated: "It is complicated in fewer instances by the 'dumping' syndrome." Butler [18] stated that dumping does not occur after the Billroth I operation. The cause of dumping is still obscure, although many theories have been advanced to explain it. We can find no significant difference between the dumping incidence or quality in the two series.

Table 9 shows that, in general, the Billroth I patients have a higher frequency of postoperative satisfaction than do the Billroth II patients. Of the Billroth I cases, in 93.5% the results are rated as satisfactory or better, as compared with only 75.0% in the Billroth II cases. Of a series of Billroth II cases at the University of Minnesota, in 89% the results are considered to be either satisfactory or excellent.

The maintenance of postoperative body weight is significantly better in the Billroth I series than in the Billroth II group (Table 8). Wollaeger [19] has shown that the loss of fat and nitrogen in the feces is less after a Billroth I resection than after a Polya modification of the Billroth II procedure.

The criticisms usually made of the Billroth I operation,[20] i.e., critical-angle (*Jammerecke*) leakage, stomal obstruction, inadequacy of resection, and inapplicability to duodenal ulcer, are not justified in the light of our series.

Certain advantages [21] of the Billroth I procedure over the Billroth II method would seem to indicate its more widespread use if it is technically feasible, and our experience indicates that it is. The advantages are as follows: 1. It is faster and

15. Wangensteen, O. H.: Personal communication to the author.

16. Muir, A.: Postgastrectomy Syndromes, Brit. J. Surg. **37**:165-178 (Oct.) 1949. Fallis and Barron.[6e]

17. Baker, J. W.: Personal communication to the authors.

18. Butler, T. J.: The Aetiology of the Early Post-Gastrectomy Syndrome, Proc. Roy. Soc. Med. **44**:775-777 (Sept.) 1951.

19. Wollaeger, F. E.: Disturbances of Gastrointestinal Function Following Partial Gastrectomy, Postgrad. Med. **8**:251-259 (Oct.) 1950.

20. Mayo.[5] Footnote 6 *a-c*.

21. Zaslow, J.: A More Physiologic Approach to Gastric Resection, Clin. Proc. Jewish Hosp. **4**:86-90 (May) 1951. Footnote 6 *a*, *b*, *c*, *f*, and *h*. Wollaeger.[19]

easier. 2. It prevents duodenal stump blowout. 3. The entire procedure is performed in the supramesocolic compartment of the abdomen. 4. The duodenum is probably more resistant to peptic ulceration than is the jejunum. 5. More nearly normal gastrointestinal function occurs. 6. Acid in the duodenum supposedly inhibits gastric secretion.[22]

## SUMMARY AND CONCLUSIONS

One hundred four patients with Billroth I and 135 patients with Billroth II subtotal gastric resections from a county hospital for a 51-month period are presented and analyzed.

The two series are compared from the standpoint of age, sex, duration of history, indications for surgery, pathology, postoperative complications, and follow-up evaluation.

Our study is compared with similar studies made elsewhere.

In our series the Billroth I procedure is being performed more frequently and the Billroth II procedure less frequently than formerly, especially for duodenal ulcer.

Data on extent of resection indicate that it is posible to do an adequate resection by the Billroth I method.

The incidence of dumping for the two series is essentially the same.

In 6.5% of the Billroth I cases the results were considered poor, in contrast with 25% of the Billroth II cases with poor results.

The over-all mortality rate for the Billroth I series is 3.8%; it is 7.4% for the Billroth II group. In cases of peptic ulcer the mortality rates are 2.2% and 8.2%, respectively.

Postoperative body weight was better maintained in the Billroth I than in the Billroth II group.

There were no recurrent ulcerations in the Billroth I series. There were three known and two possible recurrent ulcerations in the Billroth II series.

The advantages and the criticisms of the Billroth I procedure are outlined in the light of this study.

It is concluded that the Billroth I operation can and should be employed more often.

## ABSTRACT OF DISCUSSION

Dr. Alfred A. Strauss, Chicago: It is very interesting to have Dr. Harkins bring forth the subject of a comparative evaluation of the Billroth I and Billroth II operations because the Billroth I procedure, in most instances, has been completely forgotten, especially in this country. It is evident from Dr. Harkins' study that the Billroth I operation will again have to be given serious consideration.

The mortality rate of 3.8% is excellent, considering the very poor-risk patients that he has operated on. I have, for a number of years, made rounds with Dr. Harkins in the King County Hospital, and will say that I would consider the majority of patients that have had stomach resections extremely poor risks. Many of them were alcoholics; therefore I emphasize the fact that the 3.8% mortality rate is an excellent low rate considering the poor-risk patients that were operated on.

22. Pincus, I. J.; Thomas, J. E., and Rehfuss, M. E.: A Study of Gastric Secretion as Influenced by Changes in Duodenal Acidity, Proc. Soc. Exper. Biol. & Med. **51**:367-368 (June) 1942. Day, J. J., and Webster, D. R.: The Autoregulation of the Gastric Secretion, Am. J. Digest. Dis. **2**:527-531 (Nov.) 1935.

Many years ago, in the early 1920's, I spent several weeks with Dr. von Haberer, who was a great advocate of the Billroth I procedure, and I have seen him operate on a number of patients with a von Haberer-Finney modification, which is an end-to-side anastomosis. There is no question that if Dr. Harkins' series of Billroth I resections show that mechanically they function as well as the Billroth II resections, then we certainly must give the Billroth I procedure most serious consideration for the following reasons.

1. By making the anastomosis of the stomach directly to the duodenum, as in the Billroth I procedure, gastrojejunal ulcers do not occur, which is an important objection to the Billroth II or Polya procedure or its modification. When a patient who has a duodenal ulcer is subjected to a major operation like a Billroth II procedure or its modification and a gastrojejunal ulcer develops in exchange for the original duodenal ulcer, this condition is a much more serious than the lesion he had originally. Patients with gastrojejunal ulcers have almost constant symtoms, and many have repeated hemorrhages, some of which are extremely severe.

2. Another important point that Dr. Harkins brought out is that the nutrition and the weight of the patient is maintained much better with a Billroth I than with a Billroth II resection or its modification. It may be of interest that many years ago in a number of cases we did a second and third gastric resection for gastrojejunal ulcer. In each of these cases there seemed to be a regular carbuncle-type of ulcer at the gastrojejunal anastomosis. In order to avert another recurrence after a third gastric resection we made a Witzel jejunostomy through a rather large catheter and fed the patient through the Witzel jejunostomy for three to four months. In spite of the fact that we were able to feed a high caloric diet, the patient lost from 30 to 40 lb. (13.6 to 18.1 kg.). At the end of four months we fed the patient by mouth the same caloric values. The patient regained his weight very rapidly, using the same food values when fed by mouth. This would be in keeping with Dr. Harkins' observation that the patients who had a Billroth I operation, in which the food passes through the duodenum instead of the jejunum, as it does in the Billroth II, maintain and regain their weight much better. Evidently this sets up certain physiological functions of absorption in the duodenum that are absent when the food passes through the stomach into the jejunum, as it does with the Billroth II procedure, and the patients maintain their weight better than with the Billroth II operation.

3. The other interesting fact that Dr. Harkins has shown in this series is that he can do practically as high a resection as is necessary in a Billroth I operation and the amount of stomach left is no more than that left in a Billroth II, as he has shown by actual measurements of Billroth I and comparative measurements of Billroth II resections.

For years we have called attention to the fact that the size and contour of the stomach vary in persons as much as does the size of the nose. Therefore we have insisted that before the stomach is resected the wound should be retracted thoroughly in order to see the actual size of the stomach, which will then give the surgeon a much better idea how much stomach should be resected in order to leave only 30% or less.

I am rather surprised at the high percentage of mild dumping stomach syndromes in both the Billroth I and Billroth II operations. This percentage, Dr. Harkins states, is from 40 to 44%. In a series of about 1,800 resections that we have carried out for duodenal and gastric ulcer and gastrojejunal ulcers we have found a much lower percentage of mild dumping syndromes, about 10%. Again, this may be due to the difference in the type of patient that he deals with and those that we encounter.

In conclusion, I believe that (1) the Billroth I operation must be given very serious consideration if from no other standpoint than that of the absence of gastrojejunal ulcer which occurs from 1 to 5% in the Billroth II procedure, there being no question but that between 1 and 3% of gastrojejunal ulcers result from the Billroth II operation or its modification; (2) the patients with a Billroth I operation maintain their weight better than those with a Billroth II, and (3) in the Billroth I operation, as much stomach can be resected as in the Billroth II, and mechanically it functions as well as, if not better than, the Billroth II.

I think it would be fine if a number of clinics with large material would make a comparative study for a number of years comparing the value of Billroth I and Billroth II procedures, as Dr. Colp and his associates at Mount Sinai Hospital, in New York, have done in studying gastric resection with and without vagotomy.

DR. JOHN M. WAUGH, Rochester, Minn.: There are several interesting points which I should like to make. First, in any series that I know of in which the mortality in the Billroth I and II operation has been compared, the Billroth I has invariably showed a lower mortality. Yet it is difficult to understand why we have been so slow in grasping this procedure which definitely does carry a lower mortality in comparable series.

Second, Dr. Harkins has observed that there is an increased weight gain after the Billroth I as compared with the Billroth II modification, and I think this is significant because the matter of whether an operation is satisfactory depends on the end-result the patient obtains.

Third, regarding the low incidence of dumping which Dr. Harkins has pointed out, there was not an appreciable difference between the Billroth II and I procedures. Dr. Weir has recently gone over the records of a large series of gastric resection at the Mayo Clinic, and in comparing the various procedures, he also found no great difference between the Billroth I and II modifications, but the dumping syndrome occurred in about 25% of the total. These were late results, and as Dr. Strauss has pointed out, a great many of the patients will lose the symptoms within months or a year, but this study was made several years after operation and involved about 25% of the patients in the two groups. It has been my feeling, although I cannot prove it, that the patients with severe dumping, the real invalids after gastric resection, the so-called gastric cripples that Dr. Snell has written about, are more commonly seen after the Billroth II modification than after the Billroth I procedure. It is interesting to me that Dr. Harkins has been able to use the Billroth I procedure in so many cases of duodenal ulcers. We did not find it as applicable in the series reported in 1947 at the Western Surgical Association by Dr. Clagett and me, as only 5% of those patients had duodenal ulcers. However, an additional 15% had jejunal ulcers, and so actually 20% of cases were due to duodenal ulcers or their complications, 40% to gastric ulcers, and 40% to gastric malignant neoplasms.

There is one question I should like to ask Dr. Harkins. In the results he pointed out that the Billroth II procedure gave about a 12% higher excellent result than the Billroth I. That may be just a statistical decoy, so to speak, but it interested me because if that figure is accurate, there must be something in the Billroth I that we will have to follow down, or there may be some factor in the Billroth II operation which actually makes it a better operation than the figures so far would indicate. Possibly Dr. Harkins has an explanation for this.

DR. JERRY ZASLOW, Philadelphia: I feel that Dr. Harkins and his co-workers are to be commended on their vigorous approach to this problem. Although I have been doing a series of Billroth I resections which is smaller than Dr. Harkins', I have gained certain impressions which I feel are worthy of mention. The age of the patients varied from 26 to 68 years. There have been no postoperative deaths. In all patients the postoperative course was extremely benign, and the average hospital stay was eight days. In one patient a pancreatic fistula developed, which persisted for only three days and then closed completely. At no time was there any evidence of much bile regurgitation from the duodenum into the gastric remnant. I mention this because it is my feeling that many of the distressing symptoms following Billroth II resections, such as epigastric burning, anorexia, and, occasionally, bleeding from gastritis in the gastric remnant, are the result of bile and upper intestinal ferments regurgitating into the gastric remnant. With the Billroth I procedure this regurgitation does not occur, or if it does, it does so to a very slight degree. We have had only two patients that we would consider to have had the dumping syndrome. In each, the symptoms were mild and disappeared shortly after they left the hospital. In none of our patients was there any diarrhea. I must confess that our criteria for evaluating the patients were not as strict as those of Dr. Harkins.

The average weight loss from the day of admission to the day of discharge from the hospital was 8 lb. (3.6 kg.), varying from 4 to 14 lb. (1.8 to 6.4 kg.). However, that weight was regained within three weeks in all patients but one.

A complete follow-up was done in all our cases just last week. There has been no obstruction and no recurrence of ulcer or carcinoma locally. In spite of the fact that our experience with the operation has been extremely favorable, I have not been quite so vigorous as Dr. Harkins in my approach to the problem. Each patient who has a lesion in the body of the stomach or in the duodenum is subjected to resection of 75 to 80% of his stomach, including, if possible, the ulcer in the duodenum. I must confess that on numerous occasions I have felt it

unwise or unsafe to attempt to resect the ulcer in the duodenum. On these occasions the ulcer is left in place and the duodenum closed. In any other circumstance an attempt is usually made to do an end-to-end gastroduodenostomy. If this cannot be done because of tension, even after mobilizing the duodenum toward the midline, then a Billroth II operation is done. Following this plan, we have done, out of every three gastric resections, approximately one Billroth I operation. In no circumstance do we attempt to resect less stomach in order to accomplish gastroduodenostomy. Dr. Harkins has amply stressed this point.

I can assure this group that I should like to do a Billroth I operation in all cases if I were able to do it. Dr. Harkins has shown that the von Haberer-Finney modification works as well as the end-to-end operation. I have not attempted this modification, since I have not felt secure in leaving any diseased duodenum so close to a gastroduodenal anastomosis. Dr. Harkins has apparently been satisfied with the safety of this procedure, and I shall think of using it should the occasion arise.

I should like to show a few slides in order to show how extensive a resection can be done and a Billroth I anastomosis still performed.

I urge all surgeons to keep an open mind on this subject. If the surgeon would try the operation, or at least keep it in mind, I am sure he would be surprised how often it can be done with facility.

DR. M. E. STEINBERG, Portland, Ore.: Dumping is a term frequently applied in those cases in which patients have a variety of minor or major postgastrectomy disturbances, some of which have no apparent relation to the dumping syndrome.

The postgastrectomy side-effects can be arranged into several syndromes.

The afferent-loop syndrome includes the afferent-loop stasis and the afferent-loop reflux.

The afferent-loop stasis is caused by an incomplete obstruction in the proximal enteric loop. The pressure which builds up from accumulation of duodenal secretions in the proximal intestine may cause pain. A sudden peristaltic rush brings the irritating duodenal content usually into the gastric pouch, which results in gastritis, esophagitis, and vomiting of bile-stained contents.

The afferent-loop reflux is characteristic of certain types of gastrojejunal anastomoses which favor the filling of the proximal enteric segment with gastric content. A seesaw movement results which also brings the irritating duodenal contents into the gastric pouch. In my own experience with 27 patients who were subjected to corrective operations because of crippling postgastrectomy side-effects, it was found that the afferent-loop syndrome was the cause of the patient's disabilities in the greatest number of patients. In most of these patients the condition was either cured or greatly improved after a corrective operation which consisted of a gastrojejunojejunostomy (pantaloon gastrectomy).

We are all familiar with the gastric-pouch syndrome.

The afferent-loop syndrome is due to dumping. The deleterious effects from rapid entrance and passage of unprepared foodstuffs into the small bowel vary in intensity and frequency. Dumping is accepted as a compromise in all gastroenteric anastomoses, and no attempt should be made to prevent dumping. By far the greatest majority of patients with dumping fare well because of the numerous compensatory mechanisms which are set into motion. Though my limited experience with the Billroth I operation has been favorable, in a few cases corrective operations were necessary because of postgastrectomy side-effects. One can expect somewhat similar side-effects, such as precipitate emptying and reflux of pancreatic juice and bile, in the Billroth I as in the Billroth II operation.

DR. PAUL KIERNAN, Washington, D. C.: I wish to complement Dr. Harkins on his excellent work and on his extremely honest evaluation.

I wish to discuss one possible place for the use of Billroth I procedure. I think we speak too infrequently regarding those persons who have nutritional deficiency following gastric resection, whatever the method of restoration of gastrointestinal continuity employed.

Following the work of Wallaeger and Comfort, my colleagues and I have studied patients who have had gastric resection for duodental ulcers. As Dr. Strauss mentioned, the rather important point is that the duodenum seems to be needed for gastrointestinal continuity in some persons in order to gain weight after gastric resection. Therefore the possibility of a revision of the gastrointestinal continuity in the patient with serious nutritional deficiency after

a Billroth II resection was considered. We had one such patient who was studied metabolically. He was found one year after a Polya type operation to excrete huge amounts of fat and nitrogen in the feces. He also had a severe dumping syndrome. After a take-down of the Polya (gastrojejunostomy), mobilization of the previously closed duodenum, and establishment of the Billroth I type of anastomosis (gastroduodenostomy), he gained 50 lb. (22.7 kg.) previously lost, and nitrogen and fecal fat values returned to normal.

DR. I. S. RAVDIN, Philadelphia: There have been numerous references in these papers to the fact that the Billroth I operation is better than the Billroth II procedure from the standpoint of nutritional conditions of the patient subsequent to opeartion. None of those who referred to this subject have stated that the observation is not a new one, reports having appeared several times in recent years in the *Acta chirurgica scandinavica*.

DR. HENRY N. HARKINS, Seattle: I hope that I shall be able to comment on all points raised by the discussers.

The dumping syndrome has been mentioned several times, and I shall make a few remarks concerning it. In our Billroth I series we had no patients with a severe dumping syndrome, while in the Billroth II group we had two. To determine the presence or absence of the condition we ask the patient by direct question whether as a part of his postoperative course he has had sweating, palpitation, weakness, or explosive diarrhea during or immediately after the ingestion of food and if these symptoms are relieved by rest. If any of these symptoms were present at any time, the patient is classified as a "dumper." In our hospital, where the work has been done by a number of surgeons, particularly in the Billroth II group of operations, the occurrence of dumping by the criteria listed above seemed to be equally frequent as reported by the different surgeons.

Dr. Strauss has raised the question of the incidence of gastrojejunal or gastroduodenal marginal ulcer. Our follow-up studies are admittedly short in our Billroth I series, no gastroduodenal marginal ulcer having been found after resection by this technique. In the Billroth II group there are three proved and two other possible gastrojejunal ulcers, making a total of three to five such unfortunate results.

Dr. Waugh has mentioned that he has not found the procedure adaptable to most duodenal ulcers. We have surmounted this difficulty by applying the von Haberer-Finney modification of the Billroth procedure in some of the cases of duodenal ulcer which formerly we would have considered too scarred or complicated to do the original Billroth I procedure.

Dr. Waugh asks why there was 12% more excellent results in the Billroth II series. All I can say is that possibly this is a statistical aberration, but it may not be. A number of the excellent results in the Billroth II series were in patients followed for three years, and we have relatively few patients in the Billroth I series followed so long. Another factor is that in actual numbers the Billroth II group is the same. At any rate the combined percentage total of excellent and good results for the Billroth I operation is considerably greater than for the Billroth II.

Dr. Zaslow mentioned that in no instance did he have regurgitation of bile. I have no statistics to present, but it is my opinion that, by and large, regurgitation of bile is obtained from the stomach tube after either the Billroth I or the Billroth II procedure. Dr. Zaslow states that he leaves the ulcer in some cases. In our 97 Billroth I cases we removed the ulcer, if present. In the cases with the von Haberer-Finney modification we may leave the ulcer. In all instances we made the decision as to what type of anastomosis, Billroth I or II, we would make after we had made the resection, so as not to influence us as to the extent of resection. We had no complications with the von Haberer-Finney modification.

Dr. Kiernan mentions the conversion from the Billroth II to the Billroth I operation as a matter of relief for nutritional disturbances, and Dr. Ravdin referred to Dr. Perman's article in the *Acta chirurgica scandinavica* on the same subject. Dr. Perman, of Stockholm, did the conversion operation in 25 cases in which there were nutritional and other disturbances following the Billroth II procedure. He converted all 25 to Billroth I anastomoses, with 23 excellent results, 1 poor result, and 1 death following this secondary operation.

# EXPERIMENTAL GASTROJEJUNAL ULCERS PRODUCED BY REVERSING THE DUODENUM

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KALAMAZOO, MICH.
AND
EDWARD J. HILL, M.D.
DETROIT

MANY SURGICAL and chemical methods for producing ulcers in animals have been developed, but all of these preparations have had certain disadvantages.[1] None has been entirely satisfactory for studying the peptic ulcer problem in man.

All of the chemically produced ulcers, such as those caused by cinchophen and histamine in beeswax, are unsatisfactory for testing antiulcer preparations because of the theoretical drug antagonisms developing between the chemical producing the ulcer and the compound being tested.

The surgically produced ulcers also have their drawbacks. Many of them do not occur in a sufficiently high percentage of cases to make the results derived from their use of any statistical value. The Mann-Williamson preparation, consisting of an internal duodenal fistula, allows only the terminal 12 in. (30.4 cm.) of ileum to act as an absorbing area for digested food, as the entire jejunum and ileum proximal to this receive no pancreatic juice or bile to prepare the food for absorption. Because of this insufficient area the animals become cachetic. The cachexia is far advanced before an ulcer occurs in these preparations, and it kills many of the animals before ulcers develop.[2]

Dragstedt's antrum transplant produces ulcers in 80% of the animals and is a highly satisfactory preparation for studying the acute ulcer.[3] However, this ulcer does not correspond in any way to the chronic peptic ulcer observed clinically in man. The ulcer produced is a hypersecretion type which will perforate in 10 to 21 days.

We have been able to produce a more chronic type of ulcer by completely reversing the duodenum.[4] An oblique anastomosis is made between the proximal jejunal segment and the stomach, and the proximal duodenum is joined to the distal jejunal segment, again using an oblique anastomosis.[5]

1. Markowitz, J.: Experimental Surgery, Including Surgical Physiology, Ed. 2, Baltimore, Williams & Wilkins Company, 1949.

2. Hammer, J. M.; Hill, E. J., and Saltzstein, H. C.: Harper Hosp. Bull. **6**:99-103, 1948.

3. Dragstedt, L. R.; Oberhelman, H. A., Jr., and Smith, C. A.: Ann. Surg. **134**:332-342, 1951.

4. Hammer, J. M., and Hill, E. J.: Harper Hosp. Bull. **9**:129-131, 1951.

5. Poth, E. J.: Surg., Gynec. & Obst. **91**:656-659, 1950.

Mall stated that reversing a segment of the intestine, jejunum, or ileum was fatal in dogs.[6] This work was done in 1896 at The Johns Hopkins University School of Medicine on three dogs. Reports of it have remained in standard physiology textbooks since that time. However, Dragstedt was unable to confirm his conclusion,[7] and our work has not shown the reversal of a segment of bowel to be a fatal procedure.[4]

## PROCEDURE

Preoperatively the animal is starved for 24 hours except for water, then anesthetized with veterinary pentobarbital (Nembutal) sodium (Abbott) given intravenously, 1 ml. (60 mg.) per 5 lb. (2.3 kg.) of body weight. A midline or upper right rectus incision is made through the abdominal wall. After the peritoneum is opened, the duodenal ligament is cut, mobilizing the duodenum which is packed off and transected. The duodenum is then traced down to the ligament of Treitz, and the jejunum is brought into view and transected 3 or 4 in. (7.6 or 10.1 cm.) distal to the ligament of Treitz.

The proximal end of the divided jejunum is sutured to the stomach, two layers of running nonabsorbable (silk) sutures being used. The anastomosis is an oblique-to-end type, as described by Poth. This provides an adequate stoma in spite of postoperative edema of the intestinal wall. The proximal duodenum is anastomosed to the distal jejunum in the same manner (Fig. 1).

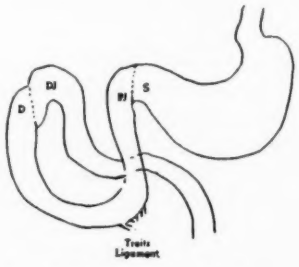


Fig. 1.—Sketch illustrating how duodenum is completely reversed, using oblique-type anastomosis. *D*, duodenum; *DJ*, distal jejunum; *PJ*, proximal jejunum; *S*, stomach.

If end-to-end anastomoses are attempted, all of the animals die in 7 to 17 days of high intestinal obstruction caused by edema and swelling of the thick musculature of the intestine. There are accompanying changes in the blood chemistry similar to those found in alkalosis. In a series of eight animals in which an end-to-end anastomosis was used, the entire group died within the stated period.

The animal is given 400,000 units of penicillin [8] intramuscularly daily for three days. Fluids are allowed ad libitum for the first 24 to 48 hours, then soft dog biscuits are given for the following 24 to 48 hours, when a regular laboratory diet is started.

In order to obtain secretion data, Heidenhain pouches were done in some of the animals before the duodenum was reversed. After a vertical midline incision approximately 4 in. (10 cm.) long was made, the stomach was brought out on the abdominal wall, and occluding rubber-shod clamps were applied across the fundus to produce an isolated Heidenhain pouch. The stomach and fundus pouch were closed in two layers with running silk sutures. A steel cannula was placed in the distal end of the fundus pouch and brought out through a stab wound in the left upper quadrant. A heavy rubber tubing or a rubber stopper was wired about the cannula to prevent its slipping backwards into the pouch and as protection for the dog's teeth. Some of

6. Mall, F. P.: Johns Hopkins Hosp. Rep. **1**:93-114, 1896.

7. Dragstedt, L. R.: Personal communication to the authors.

8. Depo-Penicillin, a product of The Upjohn Company, Kalamazoo, Mich., was used.

the Heidenhain-pouch animals with their duodenums reversed required parenteral administration of saline daily to replace electrolytes lost through the pouch by secretion of fluids containing large amounts of hydrochloric acid.

After the secretion studies were completed and the Heidenhain pouch had healed, the duodenum was reversed by opening the midline incision and carrying out the procedure previously described, except that side-to-side anastomoses were used. Such anastomoses made possible the removal of the gastric antrum for further secretion studies, as suggested by Dr. L. Dragstedt. When the antrum had been removed, the end of the stomach was closed and the secretion studies were repeated.

Direct observations were made at laparotomy on the motility of the segments under the action of methacholine (Mecholyl) bromide and epoxytropine tropate methylbromide (Pamine), as well as tetraethyl ammonium (Etamon) chloride. The methacholine bromide was used as a cholinergic agent to contract the intestinal musculature, the epoxytropine tropate methylbromide as a choline antagonist to relax and dilate it, and tetraethyl ammonium chloride as a ganglionic blocking agent.

## FINDINGS AND COMMENT

Fluoroscopic and x-ray studies following a barium meal were done on the animals with the duodenum reversed. There was a marked dilation of the stomach and duodenum, with a decided delay in emptying time. Barium was observed in the stomach four days after administration, as compared with a 2- to 4-hour emptying time in normal dogs (Fig. 2).

After ingestion of gall-bladder dye, iodoalphionic acid (Priodax), the gall bladder appeared to be dilated, but the dye was concentrated in a satisfactory manner.

A laparotomy was done on one animal a week after the duodenum was reversed, and a marked dilatation of the stomach, gall bladder, and duodenum proximal to the duodenojejunal anastomosis was found. Below this area the intestine was normal.

Because of the delay in emptying time of the stomach, it was decided that direct observations be made upon the movements of the stomach and intestine by means of a laparotomy. An animal that had had a duodenal reversal done four days before was selected. This animal had just eaten a meal of dog biscuits and water prior to surgery. He was anesthetized and the previous laparotomy incision reopened.

The stomach was moderately dilated and contained food and water. The 4-day-old anastomoses were well sealed over with a fibrinous exudate. Although the gall bladder was not distended, the duodenum was moderately distended down to the distal anastomosis between the proximal duodenum and the distal jejunum. The jejunum below the distal anastomosis was collapsed and empty.

The stomach, the reversed loop of duodenum, and the jejunal and ileal segments were packed off and brought out onto the anterior abdominal wall. There were no visible peristaltic waves in any of the intestinal segments.

At this point 3 mg. of methacholine bromide was injected into a tongue vein. The stomach contracted down almost immediately and blanched nearly white, and a peristaltic wave moved toward the reversed duodenal segment.

The duodenal segment blanched and contracted down, but there were no peristaltic waves in either direction. There was blanching in the jejunal and ileal segments, and peristaltic waves could be seen moving distally.

The effect of the methacholine bromide was of rather short duration, one to two minutes. Then the segments of intestine relaxed and the blood vessels filled again.

Fig. 2.—Comparison of upper gastrointestinal series in a normal control dog to that of one with the duodenum reversed. Note that in the control animal, top, the barium has passed completely from the stomach in two hours and appears in the colon in four hours. In the animal with the duodenum reversed, bottom, most of the barium remains in the stomach and duodenum, with only a small amount in the jejunum after four hours. Barium was demonstrated in this animal's stomach four days after the barium meal.

As soon as the effect of the methacholine bromide disappeared, 5 mg. of epoxytropine tropate methylbromide was injected into the tongue vein. The stomach relaxed and the vessels became markedly engorged. No peristaltic waves were present. The reversed duodenum and the jejunal and ileal segments showed the same reactions.

When normal color returned, 100 mg. of tetraethyl ammonium chloride was injected into the tongue vein. The stomach immediately blanched and contracted, but no peristaltic waves appeared. The same conditions were observed in the reversed duodenum and in the ileal and jejunal segments (Table 1).

TABLE 1.—*Drug Effects on Motility of Intestinal Segments in Animals with Duodenum Reversed*

| | Stomach | Reversed Duodenum | Jejunum | Ileum |
|---|---|---|---|---|
| | 3 Mg. Mecholyl Chloride (Merck) | | | |
| Blood vessels | Contraction | Contraction | Contraction | Contraction |
| Intestinal muscles | Contraction | Contraction | Contraction | Contraction |
| Peristalsis | Present | None | Present | Present |
| | 5 Mg. Pamine Bromide (Upjohn) | | | |
| Blood vessels | Engorgement | Engorgement | Engorgement | Engorgement |
| Intestinal muscles | Relaxation | Relaxation | Relaxation | Relaxation |
| Peristalsis | None | None | None | None |
| | 100 Mg. Etamon Chloride (Parke, Davis) | | | |
| Blood vessels | Contraction | Contraction | Contraction | Contraction |
| Intestinal muscles | Contraction | Contraction | Contraction | Contraction |
| Peristalsis | None | None | None | None |

TABLE 2.—*Chemistry* *

| | Before Surgery (Normal) | 1 Week After Surgery | 6 Months After Surgery | 1 Year After Surgery |
|---|---|---|---|---|
| Total proteins | 5.96 | 5.84 | 4.90 | 5.50 |
| Albumin | 4.39 | 4.37 | 3.60 | 4.17 |
| Globulin | 1.57 | 1.47 | 1.30 | 1.43 |
| A/G ratio | 2.8/1 | 2.97/1 | 2.80/1 | 2.79/1 |
| Serum chlorides | 405.6 | 420 | 575 | 575 |
| Serum sodium | 284.3 | 285 | 309 | 309 |
| Serum potassium | 10.4 | 10.1 | 15.6 | 15.6 |
| Nonprotein nitrogen | 43.5 | 44.1 | 56.1 | 54.0 |
| Carbon dioxide | 45.8 | 43.8 | 43.8 | 44.0 |

* All values are expressed in mg. per 100 cc.

Blood specimens for chemistry studies were drawn before surgery, immediately after surgery, at six months, and at one year. There was no appreciable change in the blood chemistry (Table 2).

Gastric analyses were done on all animals with Heidenhain pouches. This included animals with no surgery except the Heidenhain pouch for controls; animals with a Heidenhain pouch, the duodenum reversed, and the gastric antrum anastomosed to the distal duodenum, and animals with a Heidenhain pouch, the duodenum reversed, and the gastric antrum removed.

As shown in Table 3, the animals with reversed duodenums secreted approximately the same volume in 24 hours as the control animals, but they showed a marked increase in both free hydrochloric acid and total acid in the 24-hour observation period. This increase in acidity necessitated the replacement of electrolytes with parenterally administered saline to prevent alkalosis from developing.

In the animals with the duodenum reversed and the antrum removed, the amount of secretion was decreased to approximately 35 to 45 ml. The acidity was decreased to 10 to 12 degrees free hydrochloric acid and 16 to 20 degrees total acid. This demonstrates that the antrum had a stimulating effect on the animal with duodenal reversal and agrees with Dragstedt's experiments in which he showed that transplanting the gastric antrum to other parts of the bowel stimulates gastric secretion.

One animal was allowed to live for one and a half years, and then was inadvertently killed by another investigator. This animal had maintained its weight and was in apparent good health. Blood chemistry studies were all within normal limits. No postmortem examination was done.

Of the 10 animals killed at five and a half months, 7 had jejunal ulcers which grossly and microscopically resembled the ulcer that occurs in the Mann-Williamson animals and which showed no signs of healing.

One of these animals, in addition to having a jejunal ulcer, had an esophageal ulcer at autopsy.

At autopsy all of these animals had dilated stomachs, duodenums, and gall bladders, as was seen earlier at laporatomy and in the fluoroscopic and x-ray studies. The dilatation of the pancreatic duct, if any, was minimal at gross examination.

TABLE 3.—*Gastric Analyses*

| | Control Heidenhain Pouch | Heidenhain Pouch, Duodenum Reversed (4 Animals) | | | | Heidenhain Pouch, Duodenum Reversed, Gastric Antrum Removed (2 Animals) | |
|---|---|---|---|---|---|---|---|
| 24-hour volume | 350 ml. | 320 | 340 | 300 | 210 | 34 | 47 |
| Free HCl | 18° | 76° | 84° | 100° | 68° | 10° | 12° |
| Total acid | 53° | 122° | 116° | 132° | 108° | 16° | 20° |

## CONCLUSIONS

1. Chronic ulcers can be produced by reversing the duodenum.

2. The ulcer produced is a hyperacidity type and is not related to intestinal motility.

3. The antrum has a stimulating effect upon the gastric secretion in the animal with a reversed duodenum.

4. The duodenal reversal animal is apparently a variation of the Dragstedt antral transplant preparation.

5. Reversing the duodenum is not fatal.

6. All the intestine above the distal anastomosis of the reversed loop is dilated.

7. The reversed loop acts as a partial obstruction when the intestine is stimulated in the anesthetized animal.

8. Intestinal motility is markedly decreased fluoroscopically and on serial x-rays.

9. Animals do not lose weight.

10. Blood chemistry remains normal until an ulcer occurs.

# BLEEDING PEPTIC ULCER

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HEMORRHAGE from the gastrointestinal tract has always been a dramatic and awesome event, well known and written about in ancient times. During the past 10 to 15 years much interest has been shown in massive upper gastrointestinal bleeding. As one major hospital after another reports its results, many features have been studied intensively. Statistically, the knowledge of the frequency of massive versus mild hemorrhage, the importance of age, location of the ulcer, previous hemorrhages, diagnostic accuracy, etc., have become clarified. Old standard dictums, such as "large transfusions may blow out the clot," "the bleeding will stop when the blood pressure is low enough," "early feeding is harmful," "no patient ever dies of the first hemorrhage," etc., have been proved false and discarded. The widespread availability of large amounts of blood and the development of the modern specialty of anesthesiology have made the operations safer and the results more assured.

All institutions are critically studying their mortality figures. Much standardization has been accomplished. Reports of the past few years show a broad uniformity in the definition of what constitutes massive hemorrhage. In general, there is agreement about selection of patients for medical and for surgical treatment. There is increasing consistency in recently reported mortality statistics for large series of cases.

Nevertheless, differences of opinion do exist. There are many points in the management of bleeding peptic ulcer which are still controversial. Furthermore, the statistically reported experiences of others cannot alone constitute a guide for conduct; each case must always be considered an individual problem.

It is with the above in mind that we report the experience of Harper Hospital with bleeding peptic ulcer during the past five years, together with some personal observations on certain pertinent cases.

Table 1 shows the total number of cases of upper gastrointestinal bleeding in the record files of Harper Hospital during the years 1947 to 1951, inclusive.

There were 402 cases: 278, or 69% duodenal; 53, or 13%, gastric; 12, or 3%, marginal ulcers, and 59, or 15%, undiagnosed cases of upper gastrointestinal bleeding. During these five years there were 1,367 admissions to the hospital for

From the Surgical Service of Harper Hospital.
Dr. Lloyd Paul and Elizabeth H. Levy, B.S., assisted in this work.

peptic ulcer. Thus hemorrhage from peptic ulcer accounted for 25% of the total admissions for ulcer. The 15% undiagnosed group represents those cases in which the chart did not contain data adequately confirming the diagnosis. In many current reports there is a similar large group in which the diagnosis could not be proved. Schiff and Shapiro [1] report that the 10-year experience of Cincinnati General Hospital in upper gastrointestinal bleeding shows 20% of patients in whom the cause of the bleeding was not proved either roentgenologically or gastroscopically.

Our discussion will be confined to bleeding peptic ulcer (gastric, duodenal, and marginal), of which there were 343 cases (Table 1).

What constitutes massive hemorrhage has been difficult to define. Although in the past there has been much confusion in the reports from different institutions and in the opinions held by different clinicians, with the passage of time a considerable area of agreement has evolved. Most authors consider their clinical evaluation of the patient the best index of the severity of the disease. This includes observation

TABLE 1.—*Bleeding Peptic Ulcer (Harper Hospital, 1947 to 1951, Inclusive *)*

| Year | Duodenal | Gastric | Marginal | Total Peptic Ulcer | Undiagnosed Upper Gastrointestinal Bleeding† | Total |
|---|---|---|---|---|---|---|
| 1947 | 58 | 7 | 1 | 66 | 12 | 78 |
| 1948 | 57 | 16 | 3 | 76 | 9 | 85 |
| 1949 | 60 | 7 | 2 | 69 | 9 | 78 |
| 1950 | 57 | 12 | 5 | 74 | 21 | 95 |
| 1951 | 46 | 11 | 1 | 58 | 8 | 66 |
| Total No. | 278 | 53 | 12 | 343 | 59 | 402 |
| Total, % | 69 | 13 | 3 | .. | 15 | .. |

* Esophageal varices and carcinoma were excluded.
† Includes presumably peptic ulcer cases in which diagnosis could not be determined with certainty, e. g., no x-ray, no operation.

of the general appearance, the quality and rapidity of the pulse rate, and the drop in blood pressure, sweating, etc. Dunphy and Hoerr's [2] classification is simple, easily followed, and seems to be accepted in a very general way by many authors. It is not the amount, but the rate, of blood loss which is important.

The classification given by Dunphy and Hoerr [2] is as follows:

Group I.—Moderate; occasional syncope with onset; no disturbance of circulatory stability.

Group II.—Severe compensated, more prolonged than Group I, bled 500 to 1,000 cc. daily; circulation relatively stable.

Group III.—Severe decompensated; 1,000 to 1,500 cc. blood lost daily despite transfusion; shock prevented only by 500 cc. blood given every eight hours.

Group IV.—Exsanguinating; bleed more than 1,500 cc. in 24 hours, shock present despite more than 1,500 cc. transfusion daily.

One of the factors which the studies of the past 10 years have clarified is that the severity of the disease as seen in different types of hospitals varies. In a city hospital, with a large emergency service, more of the severe or massive hemorrhage cases are encountered. In a voluntary hospital or a private clinic in which the

1. Shapiro, N., and Schiff, L.: Ten Years' Experience with Bleeding Peptic Ulcer with Emphasis on 45 Fatal Cases, Surgery **31**:327-339 (March) 1952.

2. Dunphy, J. E., and Hoerr, S. O.: The Indication for Emergency Operation in Severe Hemorrhage from Gastric or Duodenal Ulcer, Surgery **24**:231-238 (Aug.) 1948.

patients have been previously under adequate medical care and in which the clientele consists chiefly of nonurgent cases, bleeding peptic ulcer is not, by and large, a serious disease.

Using Dunphy and Hoerr's scheme, we classified 34 of the 343 cases, or 10%, as severe hemorrhages (Group III or IV, Table 2).

Of the total 343 patients, 80% were treated medically, and the remaining 20% surgically. Of the latter, 80% were mild bleeders (Table 2). Most of them had had repeated episodes of bleeding, and the operation was an elective procedure.

The mortality was as follows: medical, 14, or 5.1%; surgical, 4, or 5.9%. These figures are not, however, comparable. Seven, or half, of the medical deaths occurred

TABLE 2.—*Medical or Surgical Treatment*

| | I | II | III* | IV* | Total |
|---|---|---|---|---|---|
| Medical | 182 | 73 | 14 | 6 | 275 (80%) |
| Surgical | 37 | 17 | 9 | 5 | 68 (20%) |
| Total | 219 | 90 | 23 | 11 | 343 |

* The total for column III plus column IV is 34, or 10%.

TABLE 3.—*Mortality*

| Group | Total Cases | I | II | III | IV | Total |
|---|---|---|---|---|---|---|
| Medical | 275 | 5 | 2 | 3 | 4 | 14 (5.1%) |
| Surgical | 68 | 0 | 1 | 1 | 2 | 4 (5.9%) |

TABLE 4.—*Causes of Death with Medical Treatment*

| Severity of Hemorrhage, Group | Total Cases | Myocardial Infarct | Cardiovascular Accident | Uncontrolled Bleeding Shock | Pulmonary | Misc.* |
|---|---|---|---|---|---|---|
| I | 5 | 3 | 1 | 0 | 0 | 1 |
| II | 2 | 0 | 1 | 0 | 1 | .. |
| III | 4 | 2 | 1 | 0 | 0 | .. |
| IV | 3 | 1 | 0 | 3 | 0 | .. |
| Total | 14 | 6 | 3 | 3 | 1 | 1 |

* Perforation peritonitis.

in the milder cases (Groups I and II), whereas three of the four surgical deaths occurred in the severer cases (Groups III and IV).

Crohn,[3] Janowitz, and others have stressed the fact that corrected statistics can be very misleading. They feel that deaths due presumably to concurrent disease (as a cerebrovascular accident or coronary thrombosis) occurring during admission for bleeding peptic ulcer should be included in the series as directly attributable to the anoxemia caused by the bleeding episode.

Table 4 lists the causes of death in 14 patients treated medically.

Note that of the 14 deaths, 9, or 64%, were caused by myocardial infarct or cerebrovascular accident.

3. Crohn, B. B.; Marshak, R. H., and Galinsky, D.: Repeated Gastro-Duodenal Hemorrhages Without Discoverable Explanation, Gastroenterology **10**:120-128 (Jan.) 1948.

Three patients died of uncontrolled bleeding. Among the 59 cases in which the diagnosis could not be proved with certainty, and which therefore were not included in the statistical analyses, there were five deaths. Three of these patients died in shock after gastrointestinal hemorrhages clinically thought to be due to ulcer.

Chinn and Weckesser [4] similarly summarized 28 medical deaths as follows: blood loss and circulatory complications, 6 (cerebral thrombosis, 3; pulmonary embolism, 1, and myocardial infarct, 2); blood loss and other complications, 13 (including carcinoma, cirrhosis of liver, tuberculosis, pneumonia, leukemia, pyelonephritis, rheumatic heart, all cases in which the acute hemorrhage merely added another burden to a serious disease state), and blood loss alone, 9 (perhaps more transfusions would have prevented these deaths). Ogilvie [5] reported 19 deaths (5.3%) in 358 consecutive admissions for massive bleeding from peptic ulcer. In eight of these cases death was due to continued bleeding, in all of which the conclusion was that transfusions were inadequate, "either too little or too late, or too little and too late." In Schiff and Shapiro's analysis of 45 fatal cases, 14 of the patients died of exsanguination.

Thus, in other recent series as in our own, there is a fair-sized group which, in retrospect, might have been saved by more vigorous transfusions.

The causes of the four surgical deaths were as follows:

1. Gastric ulcer, Group III; persistent bleeding postoperatively; massive atelectasis was cause of death.

2. Marginal ulcer, Group IV; death was due to postoperative peritonitis.

3. Duodenotomy, suture of bleeding ulcer, Group II; continued postoperative bleeding; pancreatitis was the cause of death (postmortem).

4. Marginal ulcer, Group IV; had previous gastroenterostomy; gastric resection performed; postoperatively continued bleeding from original duodenal ulcer.

### BLEEDING BEFORE AGE 45

The well-known dictum that age 45 is the dividing line and that the mortality from massive ulcer is slight before patients reach 45 is subject to many exceptions. The incidence of bleeding in the younger age group is less, but it is by no means negligible. In our series, 2 of the 18 deaths occurred in patients under 45 years of age.

Table 5 gives a few tabulations from the recent literature which shows (*A*) the mortality as related to age, with 45 being the arbitrary dividing line [6] and (*B*) the percent of severe or fatal hemorrhage occurring in persons under 45.[7]

4. Chinn, A. B., and Weckesser, E. C.: Acute Hemorrhage from Peptic Ulceration: Analysis of 322 Cases, Ann. Int. Med. **34**:339-351 (Feb.) 1951.

5. Ogilvie, A. G.; Cardoe, N., and Bentley, F. H.: Treatment of Massive Bleeding from Peptic Ulcer, Brit. M. J. **2**:304-309 (Aug. 9) 1952.

6. (*a*) Bohrer, J. V.: Massive Gastric Hemorrhage, with Special Reference to Peptic Ulcer, Ann. Surg. **114**:510-525 (Oct.) 1941. (*b*) Chinn.[4] (*c*) Schiff.[1]

7. (*a*) Hansen, J. L., and Pedersen, J.: Fatal Gastric Hemorrhages; Study of Autopsy Material Consisting of About 13,500 Cases Including 393 Cases of Hematemesis and Melena, Nord. med. **7**:1567-1574 (Sept. 21) 1940. (*b*) Cates, H. B.: Massive Hemorrhage from Peptic Ulcer: Prognosis and Treatment; Conclusions Drawn from Large Series Treated in Municipal Hospital, Ann. Int. Med. **32**:1144-1152 (June) 1950. (*c*) Holloway, J. B., Jr.; Armour, T., Jr., and Proctor, W. H., Jr.: Management of Bleeding Peptic Ulcer, Arch. Surg. **61**:487-498 (Sept.) 1950. (*d*) Brown, J. R.; Meyers, S. G.; Posch, J. L., and Deneen, O.: Massive Hemorrhage from Upper Gastrointestinal Tract: Study of 324 Cases Observed at Detroit Receiving Hospital Over 9 Year Period, ibid. **61**:767-774 (Oct.) 1950.

### HEMATEMESIS VERSUS MELENA

Meulengracht [8] first reported that hematemesis, with or without melena, had a greater mortality than melena alone. Welch [9] has recently reported a mortality for hematemesis of 20%, as against 4% for melena alone. Schiff and Shapiro,[10] on the other hand, lately reported that hematemesis carried no greater mortality than melena alone.

Our experience, in the main, agrees with that of Welch. In the total series, 50% of the patients vomited blood, and 50% had melena alone. Of the 18 patients who died, 14, or 78%, had hematemesis, while 4, or 22%, had melena alone.

### PYLORIC OBSTRUCTION AND PERFORATION

In the entire series there were five patients with concomitant pyloric obstruction. The bleeding was not massive in any of these cases. Three patients had elec-

TABLE 5.—*Seriousness of Bleeding Before and After Age 45*

| | Description of Hemorrhage | Cases No. | Before 45 | After 45 |
|---|---|---|---|---|
| A. Mortality as related to age | | | | |
| Bohrer [6a] | Severe acute hemorrhage | 548 | Mortality, gastric, 20%; duodenal, 6% | |
| Chinn and Weckesser [4] | Acute hemorrhage, (consecutive cases) | 322 | Mortality, duodenal, 5%; gastric, 9% | Total mortality, duodenal, 9%; gastric, 27% |
| Schiff and Shapiro | Over-all mortality | 510 | 4% under age 40 | 19% over age 40 |
| B. Severe or fatal hemorrhage in persons under 45 | | | | |
| Hansen and Pedersen [7a] | Fatal hemorrhage | 393 | 13% | |
| Cates [7b] | Autopsy series | ... | 8%, aged 45 or younger | |
| Saltzstein, Mahlin, and Scheinberg | Cases of bleeding peptic ulcers (343) | 18 | 2 | |
| Holloway and co-workers [7c] (Veterans Admin. Hospital, 347 cases of bleeding peptic ulcers) | Emergency surgery for uncontrolled bleeding (Group IV) | 14 | 7 were under age 45 | |
| Brown and co-workers [7d] | Severe bleeders (Groups III and IV) | ... | 33.3% | |

tive operation (resection, 2; vagotomy and resection, 1) for obstruction. Two were treated medically. Thus pyloric obstruction apparently did not increase the seriousness of the bleeding.

Five of the 343 patients had associated perforation. In four cases the operation consisted of closure of the perforation. Brief details of these cases follow: (Case A) hemorrhage two days prior to perforation; (Case B) hemorrhage one week prior to perforation; (Case C) patient bleeding before closure of perforation and continued to have bleeding for 29 days postoperatively; gastric resection was then performed as an elective procedure; convalescence was uneventful; (Case D) patient vomited blood one day.

8. Meulengracht, E.: Fifteen Years' Experience with Free Feeding of Patients with Bleeding Peptic Ulcer: Fatal Cases, Arch. Int. Med. **80**:697-708 (Dec.) 1947.

9. Welch, C. E.: Treatment of Acute, Massive Gastroduodenal Hemorrhage, J. A. M. A. **141**:1113-1119 (Dec. 17) 1949.

10. Schiff, L., and Shapiro, N.: Gastrointestinal Hemorrhage, in Sandweiss, D. J., Editor: Peptic Ulcer; Clinical Aspects, Diagnosis and Management, Philadelphia, W. B. Saunders Company, 1951, pp. 623-636.

In the fifth case the patient began bleeding after having been in the hospital for 20 days under treatment for diabetes and arteriosclerosis. He was considered to be too poor a risk for surgery and later died. The perforation was seen at autopsy. Thus another old dictum that "bleeding ulcers rarely perforate" is not true. Winters and Egan [11] reported that among patients with perforating ulcers at the Cook County Hospital there was simultaneous hemorrhage in 10% of 362 of these ulcers. Another figure from the literature is 6%.

### LOCATION OF ULCER

In Table 6 the number of deaths relative to the location of the ulcer are listed. Whereas in the total series, gastric ulcer occurs one-fifth as frequently as duodenal ulcer, deaths from gastric ulcer are almost three times as frequent as those from duodenal ulcer. This conforms with figures from the literature. Larger series show hemorrhage from gastric ulcers to be two or three times as fatal as from duodenal ulcer.

TABLE 6.—*Deaths Relative to Location of Ulcer*

| | % of Total Cases | Total No. Cases | Total Deaths | % Deaths | Surgical Treatment | Medical Treatment |
|---|---|---|---|---|---|---|
| Gastric | 16 | 53 | 6 | 11.3 | 1 | 5 |
| Duodenal | 84 | 278 | 11 | 4.0 | 2 | 0 |
| Marginal | .. | 12 | 1 | .... | 1 | 0 |
| Undiagnosed | .. | 59 | .. | .... | 0 | 5 |

### MORTALITY: FIRST EPISODE VERSUS SUBSEQUENT EPISODES

Is the first episode more likely to be fatal than subsequent episodes? Our experience in the 18 cases is as follows:

| Group | Died After First Episode | Died After More Than One Episode |
|---|---|---|
| I | 4 | 1 |
| II | 3 | 0 |
| III | 2 | 3 |
| IV | 1 | 4 |
| Total | 10 (56%) | 8 (44%) |

Thus 10 of the 18 deaths occurred in the first episode and eight in subsequent episodes. However 7 of the 10 deaths in the first episode occurred in mild bleeders. This means that in many instances the patient had an associated condition, and death was probably due to the anoxia caused by the hemorrhage. In evaluating the severer bleeders, 7 of the 10 patients who died in Groups III and IV had bled more than once.

### LABORATORY TESTS

Many patients entered the hospital with a red blood cell count of less than 3,000,000 and a hemoglobin level of less than 50% and yet were not in shock. These patients had been slowly bleeding over a prolonged period and had become physiologically adjusted to the lowered blood volume.

11. Winters, W. L., and Egan, S.: Incidence of Hemorrhage Occurring with Perforation in Peptic Ulcer, J. A. M. A. **113**:2199-2204 (Dec. 16) 1939.

Lipp and his associates [12] reported several instances of death occurring in patients with red blood cell counts in excess of 3,000,000. In our series 11 of 18 patients who died had blood counts of over 3,000,000 red cells. Six of these 11 patients were considered to have massive hemorrhage.

It is well recognized that early hemoglobin values and red blood cell counts may be inaccurate as indications of the severity of the bleeding. (The same holds true for pulse rate and blood pressure.) For the first two hours after the onset of bleeding, there will be no change in the blood cell count. Twenty-four to 48 hours are required for the restoration of fluid volume (Ivy and Grossman [13]), and only after 72 hours will the lowest level of red blood cell distribution and hemoglobin be reached. Wallace and Sharpey-Shafer (cited by Cates [7b]) bled normal convalescent patients an average of 1,150 cc. It took 3 to 90 hours for hemoglobin to reach maximum dilutions, the average being 32 hours.

Blood volume determinations by the Evans blue dye or radioactive methods, though used by some, have not become popular. We have tried the Evans blue dye test. Although otherwise simple to perform, the blood must be drawn quite accurately, necessitating the services of an experienced technician; also the test is expensive, and sometimes it is hard to correlate the data with the patient's statement of his previous normal weight. We agree with the majority of recent writers that while the test is desirable, the patient's condition can be properly evaluated without it.

## TREATMENT

It is becoming recognized that the aim in treatment of upper gastrointestinal hemorrhage consists, to a large degree, in averting the ill effects of anoxia upon the body economy. Some recent experimental work by La Veen, Mulder, and Prokop [14] has shown that bleeding from the gastroduodenal artery will cause the blood pressure in the hepatic artery to fall much more rapidly than will the same amount of blood lost from the peripheral circulation, such as the femoral artery. This selective reduction of blood flow is greatest when systemic blood pressure reaches levels below 100 mm. Hg.

Anoxia can be produced very easily in the liver. Although 75% of the blood supply of the liver is derived from the portal vein, 50% of its oxygen supply comes from the hepatic artery. Even in early shock, the portal vein is quickly drained of

12. Lipp, W. F.; Lipsitz, M. H.; Milch, E., and Aaron, A. H.: Management of Massive Hemorrhage from Gastroduodenal Ulceration, J. A. M. A. **145**:14-16 (Jan. 6) 1951.

13. Ivy, A. C.; Grossman, M. I., and Bachrach, W. H.: Peptic Ulcer, Philadelphia, The Blakiston Company, 1950, pp. 567, 572.

14. La Veen, H. H.; Mulder, A. G., and Prokop, F.: The Physiological Mechanism for Death in Massively Bleeding Peptic Ulcer, Surg., Gynec., & Obst. **94**:433-442 (April) 1952. With a cannula tied in the gastroduodenal artery of a dog, and one in the left femoral artery, these workers produced rapid bleedings from each of these vessels, meanwhile measuring the blood pressure and blood flow in the hepatic artery and in the peripheral circulation (femoral artery). When the bleeding was from the gastroduodenal artery, the hepatic artery pressure dropped to 50 mm. Hg, while the femoral artery pressure was maintained at 75 mm. Hg. This differential was not noted when the bleeding was from the femoral artery. Measuring the blood flow instead of the blood pressure, the difference was more striking. During rapid gastroduodenal bleeding, at the time when the hepatic flow has completely ceased, the femoral artery blood flow is reduced only by one-third. The hepatic blood flow ceases entirely when the hepatic artery blood pressure is about 60 mm. Hg.

its oxygen saturation (which is normally 20% less than that of arterial blood), and the liver is dependent upon the hepatic blood flow for its entire oxygen supply. Complete occlusion of the hepatic circulation for one hour or more produces irreversible liver damage. The ill effects of anoxia upon the myocardium and brain are also well known. Amendola [15] has made the observation that a patient who is persistently bleeding and continues to have deep penetrating "ulcer pains" will often show acute coronary insufficiency if an electrocardiogram is taken. He thinks that the myocardial ischemia and anginal pain are due to the anoxia and hypotension of the continued blood loss.

### DELAYED SURGERY

Although in some clinics (Stewart [16]) laparotomy is performed immediately for massive bleeding, the principle that the rate of bleeding is the important factor is becoming, in a general way, a guide to clinical observation and treatment. In our experience, if a patient can be kept out of shock, with circulation well stabilized as indicated by the pulse rate and blood pressure, he is not in danger. After an initial blood replacement of 500 to 1,500 cc. or more (depending on the severity of the hemorrhage), 500 cc. of blood is given every eight hours. This is the plan of management laid down by Dunphy and Hoerr. If plenty of blood is available and the patient is not becoming depleted, the need for surgery is not immediately urgent. The rule that this decision must be made in 36 to 72 hours is subject to many exceptions. If a patient can be tided over the acute hemorrhage and his blood volume and hemoglobin level restored to normal, he is a far better surgical risk.

At times, we have delayed the decision to operate for several days, especially when there are complications such as marked obesity or hypertension. Provided adequate blood replacement is given and the patient is very carefully observed, no harm results from the delay.

CASE 1.—A very obese stocky woman, aged 56, bled continuously by slow ooze for one week. She was never in shock. Five hundred cubic centimeters of blood was given daily to maintain the hemoglobin level, not for shock. Because of the technical difficulties anticipated, operation was delayed. When bleeding continued after seven or eight days, gastrectomy was performed. A large posterior ulcer was found which was eroding into the pancreas.

At Presbyterian Hospital, New York, (Porter [17]), in 1948, there were 76 patients with massive hemorrhage from ulcer (defined as "rapid enough to have obvious constitutional effects"): 45 were treated conservatively; 16 were first treated conservatively then operated upon after an average stay in the hospital of three to four weeks before operation, and 15 had emergency operations. In the conservatively treated group there was one death from a cerebrovascular accident in a patient who had already had one stroke. In MacKinnon's [18] series, 74% of his

15. (*a*) Amendola, F. H.: Surgical Intervention in Massive Gastroduodenal Bleeding, Surgery **31**:340-348 (March) 1952; (*b*) Management of Massive Gastroduodenal Hemorrhage, Ann. Surg. **129**:47-56 (Jan.) 1949.

16. Stewart, J. D.; Schaer, S. M.; Potter, W. H., and Massover, A. J.: Management of Massively Bleeding Peptic Ulcer, Ann. Surg. **128**:791-802 (Oct.) 1948. White, W. C., in discussion on Stewart and others. Stewart, J. D.; Massover, A. J.; Potter, W. H., and Schaer, S. M.: Massive Hemorrhage from Gastroduodenal Ulcer, Surgery **24**:239-245 (Aug.) 1948.

17. Porter, M.; Harvey, H. D., and Schullinger, R. N.: Massive Hemorrhage from Peptic Ulcer, Arch. Surg. **60**:1076-1092 (June) 1950.

18. Mackinnon, D. C.: Surgical Management of Massive Hemorrhage from Gastric and Duodenal Ulcers, Minnesota Med. **33**:244-254 (March) 1950.

patients with acute massive hemorrhage from ulcer were operated upon after 48 hours had passed. Loe[19] reported 94 cases of massive hemorrhage from the Swedish Hospital in Seattle, of which 69 were from ulcer. Medical treatment was employed in 52 of these cases, with 1 death; in 17 operation was performed, with no deaths. Only three operations were done in the first 48 hours.

There are exceptions to all rules. In the following case, perseverance in continuing transfusions avoided a difficult laparotomy.

CASE 2.—A man, aged 38, had a gastric resection for duodenal ulcer two years before by an experienced surgeon in Toronto. He suddenly had very profuse hemorrhage. Twenty-two pints (11 liters) of blood were given over a period of 14 days. We then became worried and advised operation. Another consultant advised further delay because the patient's circulatory status was being maintained. After five more days passed, and a total of 28 pt. (14 liters) of blood were given, the patient stopped bleeding. He has been well since then (three years), without any ulcer symptoms, and is able to carry on an active salesman's job which requires much travelling.

Heuer (cited by Levison) reported on one patient who had 59 massive upper gastrointestinal hemorrhages over a 25-year period and finally died of intracranial hemorrhage.

Dr. D. J. Sandweiss has told me of a patient of his, a woman now aged 45, who has had a duodenal ulcer since 1925 (27 years). She had bleeding in 1927, 1928, 1929, 1934, 1941, 1944, 1945, and 1946. Most of these episodes consisted of melena only, but she required hospitalization five or six times for hemorrhage. There has been no further hemorrhage or other symptom since 1946 (six years ago). Another of his patients, a woman now aged 71, has had a duodenal ulcer since 1928 (24 years). She had hemorrhage in May, 1928; October, 1929; March, 1930; May, 1932; December, 1933, February, 1934, and March, 1934. All of these episodes were melena, and she was never in the hospital for them. She has been perfectly well since then except for hypertension (18 years).

The cases in which hemorrhage is most treacherous are those in which bleeding lasts for a few days, then stops, then starts again, especially if shock ensues each time. These patients are bleeding from an open vessel in the posterior wall of the duodenum and are likely to suddenly have hemorrhage.

CASE 3.—A large, heavy, Negro woman, aged 43, with a hypertension of 240/120, was admitted on Sept. 2, 1949, for observation of upper abdominal pain radiating to the right portion of the back, of six or seven years' duration. On the eighth day after admission, following an x-ray examination of the gastrointestinal tract, her systolic blood pressure dropped from 230 to 104. The administration of 1,500 cc. of whole blood restored it to normal. Then she stopped bleeding for two days but started again, with the blood pressure dropping from 230 to 70/50. She went into shock and was cold and clammy. This time, 500 cc. of blood restored her blood pressure to normal. During the next two days she required 500 cc. of blood every eight hours to maintain normal blood pressure. The tarry stools continued. She was operated upon Sept. 17, two days after recurrence of the hemorrhage. A large duodenal ulcer of the posterior wall was found penetrating into the pancreas. Subtotal gastrectomy was performed. She has remained well for three years. The hypertension is now much less.

Such patients (recurrent bleeders) should be operated upon before leaving the hospital because they may suddenly start to bleed a long time after discharge, and

19. Loe, R. H.: Massive Hemorrhage in Upper Part of Gastrointestinal Tract: Emphasis on Atypical Type, Arch. Surg. **61**:183-192 (July) 1950.

the subsequent hemorrhage may be fatal. There is unanimity of this opinion throughout the recent literature. The following case convinced us of this fact in a dramatic manner.

CASE 4.—A slim woman, aged 40, was admitted on Dec. 26, 1947, for bleeding peptic ulcer, under the care of Dr. R. H. Connelly. There was only a slight blood pressure drop from her normal of 110/78 to 98/68. She responded to the administration of 1,000 cc. of whole blood but felt weak for the next few days.

On Jan. 3, 1948, she suddenly began bleeding again. Within 12 hours the blood pressure dropped to 66/30, and her extremities were cold. Blood was started into both antecubital veins. Preparations were made for emergency operation if necessary, but in another 12 hours and after 2,500 cc. of blood was given, her blood pressure was 110/70, pulse rate 90 beats a minute, and she was alert and happy. After another two weeks of ulcer management in the hospital, during which time she felt well, she was discharged. She had several personal and marital adjustments to make and was told that her condition warranted one more trial of medical management, with the understanding that operation would be indicated if she continued to have distress or pain.

For the next four months, except for some lower abdominal cramps and complaints of nervousness and insomnia, she was well. She was under close medical observation and gained 4 lb. (1.8 kg.).

On April 5, 1948, suddenly at 1:00 a. m., she began having signs of bleeding, with vomiting and weakness. She was rushed to the hospital by ambulance. Although conscious at the time of leaving home, she was practically moribund on arrival at 3:30 a. m., and she died a few minutes later. Autopsy showed a duodenal ulcer penetrating into the head of the pancreas, with marked arteriosclerosis of the vessels in the region of the pancreas.

The other group with serious bleeding, alluded to by several writers, are those patients in whom bleeding starts while they are under strict hospital medical treatment for uncomplicated ulcer.

### PREVIOUS ULCER HISTORY

It is not necessary to have a long or even a recent history of peptic ulcer to have massive hemorrhage from it. This is especially true in persons past 60 (Cates [7b]).

In the 10-year experience of the Cincinnati General Hospital (Schiff and Shapiro), 34, or 10%, of 339 patients with proved cases of bleeding peptic ulcer had no history of any digestive distress prior to the hemorrhage. In Chinn and Weckesser's series, 17% had "no history suggestive of peptic ulceration prior to onset of acute hemorrhage." Ivy, Grossman, and Bachrach,[13] list a table of 1,678 collected cases of hemorrhage from peptic ulcer. In 16.2% of these cases the patients had had no previous symptoms.

In the following case, the exhaustion, perhaps the adrenal stress [20] of the two operations, with no bowel movement for seven days, was apparently sufficient to reactivate an ulcer which had been dormant for 26 years.

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20. McDonnell, W. V., and McCloskey, J. F.: Acute Peptic Ulcer as a Complication of Surgery, Am. Surg. **137**:67 (Jan.) 1953. These authors have recently reported eight cases of acute peptic ulcer found at autopsy in patients dying within two months of various general surgical operations (gall bladder [2 patients], carcinoma of ovary, fracture hip, thigh amputation for circulatory disease, bladder resection, pneumonectomy). Three of these patients had shock and three others had postoperative infections. The statistical incidence was higher than that for similar acute peptic ulcers following central nervous system lesions. Acute peptic ulcer, they feel, is "simply one result of the body's exposure to stresses." Infection, shock, etc., increase the secretion of corticotropin. Corticotropin administration might aggravate the symptoms of peptic ulcer.

CASE 5.—A man, aged 65, had an abdominoperineal resection for carcinoma of the rectum. On the seventh day postoperatively, laparotomy had to be performed for a small bowel obstruction. His colostomy began to function properly two days after this second operation. Suddenly, after another 24 hours he began to bleed copiously from the gastrointestinal tract. Bright-red blood poured from the colostomy. During the next three days 21 pt. (10.5 liters) of blood were given, but profuse hematemesis and bleeding from the colostomy continued. Fresh blood poured from the colostomy stoma. The only ulcer-like history which could be obtained was that 26 years previously he had been treated for ulcer-like distress but had had no similar symptoms since then. He had been a steady and moderately heavy whiskey drinker all his life. He was considered too sick to transport to the x-ray department; consequently, the source of the hemorrhage could not be ascertained. (The use of a Patton balloon did not stop the bleeding.) He was finally taken to the operating room in only fair condition. A few minutes after a gastrotomy incision was made in the distal stomach, blood spurted 1 ft. (30 cm.) from this wound. There was a large dense duodenal ulcer penetrating into the pancreas. Several sutures were placed in the pancreas bed, the duodenal stump closed as well as possible, and a subtotal gastrectomy done. He convalesced satisfactorily. At present, 12 months after the operation, he has no gastric symptoms, and his colostomy functions well.

In such cases an intra-arterial transfusion may be of value. This method will bring the coronary pressure from shock levels to normal in one-fourth the time required when rapid intravenous transfusion is used (Letton [21]).

We have not had occasion to use intra-arterial transfusion in bleeding peptic ulcer but have found it a dramatic and lifesaving measure in four other situations.

## DIAGNOSIS

Accurate diagnosis is one of the present-day problems in the surgery of massive upper gastrointestinal hemorrhage. Most observers feel that x-ray examination during bleeding is not dangerous if no abdominal pressure is applied. We have not hesitated to use it. The esophageal balloon may help establish the diagnosis, in that if hemorrhage ceases, the cause was probably bleeding esophageal varices.

In our series, 59 patients, or 15%, had undiagnosed upper gastrointestinal bleeding. A certain small percentage of patients will come to operation with the bleeding undiagnosed (portal hypertension excluded), and even at operation no ulcer will be found. On making an incision into the stomach, no definite ulcer is seen, but there is massive bleeding inside the stomach.

CASE 6.—This patient had been bleeding for several days, while under observation in the hospital, and his condition in spite of multiple transfusions was critical. At laparotomy, no gross ulcer was seen. A 2 in. (5 cm.) incision into the stomach disclosed a massive oozing mucosal surface. Many large firm clots were sponged out of the interior of the stomach and the gastrotomy incision closed. The left gastric artery was ligated, and the abdomen was closed.

The patient stopped bleeding and convalesced without incident. He lived four years postoperatively, during which time there was no further bleeding. He died of a brain tumor.

Such cases pose a problem about which there is a difference of opinion as to management. The majority of surgeons who write on bleeding peptic ulcer advise immediate gastrectomy in such a situation and for the following reasons: 1. The ulcer may be so small that it is not detected by the fingers at operation. Such an ulcer can be responsible for fatal hemorrhage (Downie [22]). At autopsy there will

21. Letton, A. H.: Exsanguinating Peptic Ulcer, Am. Surgeon **17**:876-878 (Sept.) 1951.

22. Downie, V. J.: Massive Haemorrhage from Acute Gastric Ulcer, Brit. M. J. **2**:24-25 (July 5) 1952.

be a small superficial erosion with a sclerotic artery in the base (Wangensteen [23]). 2. There may be a low-lying duodenal ulcer which cannot be felt until the pancreas is separated away. 3. There may be arterial thrombosis in a gastric erosion or a small clinically undetectable aneurysmal varix (Cole [24]). 4. There may be a diffuse acute gastritis (the most frequent finding) with a large surface of superficially eroded mucosa (Schindler [25]). Ogilvie states that in such a situation intragastric exploration is unsatisfactory, for "it is impossible to search adequately all the large potential areas of bleeding." He reported having done gastrectomy in seven instances in these circumstances, and in only one case did the bleeding continue after operation.

The contrary opinion is that if an immediate gastrectomy is done when no bleeding point is found "too many errors may be made . . . . and the resection will be done for obscure lesions outside the area resected" (Cole [24]).

Others likewise feel that it is not justifiable to do a gastrectomy unless a definite source of the bleeding can be found. Amendola recommends a long incision throughout the entire length of the anterior surface of the stomach extended into the duodenum, exposing the entire gastric mucosa, to find the source of bleeding before deciding to do a gastrectomy.

A few instances culled from the recent literature, reporting such errors of judgment, follow:

1. Holloway [7e]:

A subtotal gastrectomy was done for massive uncontrolled bleeding in a patient with the presumptive diagnosis of bleeding duodenal ulcer, but later investigation revealed a bleeding polyp of the colon.

We personally know of another similar case in which several months after gastrectomy for undiagnosed bleeding the ascending colon was removed because of continuation of the bleeding, and a small polyp which had bled severely was found in the specimen.

2. Loe [19]:

After the patient's fourth admission to the hospital for bleeding, the source of the bleeding was localized 1 ft. (30 cm.) beyond the pylorus by continuous aspiration after gradual introduction of a Miller-Abbott tube. At operation a leiomyoma of the jejunum was found.

3. Amendola [15a]:

The bleeding point was found in the residual gastric pouch just as the gastrojejunal anastomosis was about to be done.

4. Amendola [15a]:

In another case a small post-traumatic aneurysm was found ruptured into the third portion of the duodenum, after a long gastrotomy incision had not demonstrated any bleeding points.

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23. Wangensteen, O. H.: Ulcer Problem: Etiology with Special Reference to Interrelationship Between Vascular and Acid-Peptic Digestive Factors; Characterization of Satisfactory Operation Which Will Protect Against Recurrent Ulcer (Listerian Oration), Canad. M. A. J. **53**:309-331 (Oct.) 1945.

24. Cole, W. H.: Symposium on Gastroesophageal Surgery: Surgical Treatment of Bleeding Peptic Ulcers, S. Clin. North America **31**:271-283 (Feb.) 1951.

25. Schindler, R.: Gastroscopy: The Endoscopic Study of Gastric Pathology, Chicago, Chicago University Press, 1937.

### HEMORRAGE AFTER RESECTION

In our series, three of the four patients who died after surgery bled postoperatively. In our personal experience we have had a few patients bleed moderately, but not seriously, after resection for bleeding duodenal ulcer. Another case, which ended fatally, is the following:

CASE 7.—We were called to another hospital by a competent surgeon to see a patient who was bleeding from the gastrointestinal tract (both vomiting and melena) following gastric resection for bleeding duodenal ulcer. After a few days of conservative treatment, including several transfusions, the hemorrhage did not stop, and the patient was reexplored. Unable to determine the source of the bleeding and thinking it was probably from the anastomotic line, a resection was done. The stump of the duodenal closure was investigated, but it was thought that there was not sufficient indication to explore it completely. The patient recovered from the operation but continued to bleed and died in another five to six days. Postmortem examination showed a large open vessel in an indurated and calloused duodenal ulcer.

Porter is very specific regarding this point.

If there is hemorrhage after operation, the presumption is that it comes from the ulcer bed rather than the suture line, although the latter on rare occasions can be the source. Do a second operation, and go straight to the duodenal stump.

### SUMMARY AND CONCLUSIONS

Four hundred and two cases of massive upper gastrointestinal hemorrhage, comprising five years' experience (1947 to 1951) at Harper Hospital, are reviewed. There were 343 cases of peptic ulcer (69% duodenal, 13% gastric, 3% marginal) and 59 cases, or 15%, of undiagnosed upper gastrointestinal bleeding.

Hemorrhage from peptic ulcer accounted for 25% of all admissions for peptic ulcer.

Of the hemorrhages from peptic ulcer, 10% were severe (shock being prevented only by the administration of 500 cc. blood every eight hours, or uncontrollable hemorrhage resulted).

Of the 343 patients, 80% were treated medically and the remaining 20% surgically. Of those treated surgically, 80% were mild bleeders. Many of them had bled previously.

There were four, or 5.9%, surgical deaths.

The medical mortality was 5.1%. Half these deaths occurred in mild bleeders, several of whom had associated cardiovascular conditions. The anoxia of gastrointestinal hemorrhage may have precipitated cardiovascular accidents.

Three of the 14 patients who died while under medical management died in shock of uncontrolled hemorrhage. Several series reported recently contain an appreciable number of fatal cases in which more vigorous transfusions might have been lifesaving.

Two of the total 18 deaths occurred in patients aged 45 or under.

Of the total number of patients (343 with peptic ulcer) 50% had hematemesis; 50% had melena alone. Yet of the 18 who died, 14, or 78%, had hematemesis and 4, or 22%, had melena alone. Therefore hematemesis has a more serious prognosis than melena alone.

Pyloric obstruction did not increase the seriousness of the bleeding.

Five of the 343 patients had associated perforation. In some series as many as 10% of the bleeding ulcers perforated.

Deaths from bleeding gastric ulcer was three times as frequent as those from duodenal ulcer.

About half of the fatalities occurred during the first episode of bleeding.

The treatment of massive upper gastrointestinal hemorrhage consists, to a large degree, in giving sufficient blood to prevent the ill effects of anoxia upon the liver, primarily, and also upon the myocardium and the brain.

The decision to operate does not necessarily have to be made in 48 or 72 hours if the patient can be maintained without anoxia. There is a great advantage in bringing the patient to operation with anemia, blood loss, and electrolyte imbalance, etc., corrected.

Patients with the most treacherous bleeding are those in whom there is repeated bleeding with a drop in blood pressure while under observation. These patients should be operated upon before leaving the hospital, because of the likelihood of sudden fatal hemorrhage occurring even months afterward.

Of the patients with acute hemorrhage from peptic ulcer, 10 to 15% have no ascertainable previous history of ulcer. This is especially true of older patients. They may have profuse upper gastrointestinal bleeding while in the hospital and under treatment for some unrelated serious operation or illness.

In spite of all diagnostic procedures, a small number of these patients will come to operation with the bleeding undiagnosed, and at exploration of the interior of the stomach and duodenum no ulcer will be found. It is not necessarily the best surgical judgment to resect the stomach if no bleeding point is found.

Uncontrollable postoperative hemorrhage following resection presents a serious problem. It frequently comes from the duodenal stump but may come from the anastamotic suture line and sometimes may be relieved by manually evacuating large clots from the residual gastric stump. This may allow the stomach to contract sufficiently to arrest the bleeding.

# PERIPHERAL EMBOLIZATION FOLLOWING MITRAL COMMISSUROTOMY

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PERIPHERAL emboli usually arise in the heart as a result of underlying cardiac pathology. They occur in rheumatic heart disease (rheumatic mitral stenosis almost exclusively) following coronary occlusion, in arteriosclerotic heart disease with auricular fibrillation, and as a result of bacterial endocarditis. Rarely, a paradoxical embolus of venous origin may pass an abnormal major venous-arterial shunt and lodge peripherally.

The advent of the operation of mitral commissurotomy for mitral stenosis, with its attendant intracardiac manipulation, has introduced another major cause for arterial embolization. In many cases of mitral stenosis there are thrombi filling the left auricular appendage through which the finger is placed to correct the valvular lesion. These thrombi may be old, firm, fibrotic, and adherent, in which case the danger of embolization is minimal, or they may be fresh, soft, and poorly attached with a marked tendency to break off and lodge somewhere in the peripheral arterial tree. Emboli may also arise during commissurotomy from the valve leaflets. Patients with long-standing mitral stenosis often have calcium deposits on the valve. During commissurotomy one or a shower of calcium emboli may be discharged into the circulation. These calcific emboli, being small, are more likely to occlude smaller vessels. In a recent article, Bolton, Maniglia, and Massey [1] report a case of calcific embolus to the cerebral vessels following mitral commissurotomy.

In a series of 901 mitral commissurotomies performed in the thoracic surgical service of the Hahnemann Medical College and Hospital by Drs. Bailey, Glover and O'Neill, there were a total of 28 emboli, 19 of which were cerebral and 9 peripheral. The latter included two at the aortic bifurcation, five common femoral, one axillary, and one common carotid.

In an attempt to reduce the incidence of cerebral emboli, Bailey and his associates [2] advocate a new technique of temporary occlusion of the major vessels to the head and neck during the act of cutting the mitral valve. If this technique

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1. Bolton, H. E.; Maniglia, R., and Massey, F. C.: Calcific Emboli Complicating Mitral Valve Commissurotomy, J. Thoracic Surg. **24**:502 (Nov.) 1952.

2. Bailey, C. P.; Olsen, A. K.; Keown, K. K., and Nichols, H. T.: Commissurotomy for Mitral Stenosis: Technique for Prevention of Cerebral Complications, J. A. M. A. **149**:1085 (July 19) 1952.

is successful in accomplishing its purpose, we can expect to find a higher number of emboli lodging in the major peripheral vessels, where early diagnosis and direct surgical attack can readily be accomplished.

Abanejew [3] unsuccessfully attempted the first arterial embolectomy in 1895. The first successful embolectomy was reported in 1911 by Leahy.[3] Since then the removal of peripheral arterial emboli, with preservation of life and limb, has been accomplished numerous times.

The surgical management of emboli to the aortic bifurcation, however, has met with much less success. The medical literature contains 41 case reports [4] of successful aortic bifurcation embolectomies accompanied by complete restoration of circulation to the lower extremities.

Bloomberg, Blumberg, and Haimovici [4h] reported the 41st successful aortic bifurcation embolectomy following left auricular appendage and chamber exploration for removal of a thrombus, at which operation an incidental mitral commissurotomy was performed.

This paper presents, in addition to a discussion on peripheral embolization following mitral commissurotomy, the report of the 42d successful aortic bifurcation embolectomy, this case following mitral commissurotomy for the cure of mitral stenosis.

## REPORT OF A CASE

A. M., a 27-year-old white man, was admitted to the cardiac surgical service of Dr. Thomas J. O'Neill on Jan. 2, 1952. The patient gave a history of two episodes of scarlet fever in his childhood but no frank rheumatic fever. He was in relatively good health until 1947, when progressive exertional dyspnea was noted. In 1948 an episode of frank cardiac decompensation occurred which, however, responded well to the administration of digitoxin and mercurials. In 1949 auricular fibrillation developed, and this has persisted to date. Embolization to the left popliteal artery occurred in 1949, and responded well to conservative therapy. A splenic infarct was diagnosed in 1951. In December, 1951, hemoptysis developed and has persisted. His exertional dyspnea had progressed to the point where walking one-half block produced distressing pulmonary symptoms. A weight loss of 35 lb. (15.9 kg.) had occurred since 1947.

The physical examination on admission disclosed a pale white man. The blood pressure was 104/70. The radial pulse rate was 82 beats a minute and grossly irregular. The point of maximal impulse in the fifth left interspace was 9.5 cm. from the midsternal line. A grade 2 to 3 high-pitched musical systolic mitral murmur was present and was well heard in the axilla and back. A grade 3 mitral diastolic rumble accompanied by a thrill was also present. $M_1$ and $P_2$ were accentuated. The lungs were clear. The liver edge was enlarged 5 cm. below the right costal margin and was tender. The spleen was just palpable. No pedal edema was noted. Dorsalis pedi pulses were present bilaterally.

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3. Abanejew, cited by Burgess, C. M., and Hartwell, A. S.: Removal of Saddle Embolus of Aorta, J. A. M. A. **141**:387 (Oct. 8) 1949.

4. (*a*) Thiessen, N. W., and Marxen, N. L.: Successful Direct Aortic Embolectomy, Am. J. Surg. **84**:358 (Sept.) 1952. (*b*) Oudot, J.: Embolie post-opératoire de la fourche termino-aortique: Embolectomie de suites heureuses, Mem. Acad. chir. **77**:794 (Oct.) 1951. (*c*) Wells, J. J., and Denneen, E. V.: A Successful Embolectomy for a Saddle Embolus of the Abdominal Aorta, U. S. Armed Forces M. J. **2**:763 (May) 1951. (*d*) Wolff, J. P.: Successful Embolectomy at Bifurcation of Aorta, South. Surgeon **15**:545 (Aug.) 1949. (*e*) Pool, R. M., and Farrar, T.: Aortic Embolectomy, Ann. Surg. **135**:655 (May) 1952. (*f*) Ewing, M. R.: Aortic Embolectomy, Brit. J. Surg. **38**:44 (July) 1950. (*g*) Shipman, J. J., and Goodwin, J. F.: Saddle Embolus of the Aorta, Lancet **2**:133 (July 28) 1951. (*h*) Bloomberg, A. E.; Blumberg, P., and Haimovici, H.: Auricular Thrombosis, Mitral Commissurotomy, and Aortic Embolectomy: Report of a Case, A. M. A. **150**:1216 (Nov. 22) 1952.

Except for a normocytic anemia and a reduced prothrombin level, the blood studies were within normal limits. The electrocardiogram was read as showing auricular fibrillation, right axis deviation, and digitalis effect. The roentgenologic cardiac survey showed cardiac enlargement consistent with mitral stenosis.

On Jan. 9, 1952, at 10:00 a. m. a mitral commissurotomy was performed on a markedly stenosed and calcified mitral valve. At surgery the left auricular appendage through which the commissurotomy knife was to be passed was felt to be full of soft thrombi. In order to reduce the possibility of embolization, an O'Neill clamp was placed across the base of the appendage and an opening into it made and all visible clots evacuated prior to the insertion of the examining finger. The commissurotomy was then performed without incident.

At 12:30 p. m. (Jan. 9) the patient complained of severe pain and numbness of the legs and feet. Examination at this time revealed the legs and feet to be cold. The femoral, popliteal, and dorsalis pedi pulses were absent bilaterally. A diagnosis of saddle embolus of the aorta was made, and continuous caudal anesthesia, using 0.4% beta-diethyaminoethyl para-ethoxy benzoate hydrochloride (Intracaine), was started at 1:30 p. m. There was no relief of pain and no improvement in the circulation of the lower extremities.

At 3:30 p. m. (Jan. 9) with use of continuous caudal anesthesia of 1% Intracaine, the patient's abdomen was opened through a left transrectus incision. Aortic pulsations ceased at the bifurcation and soft clot could be felt at the bifurcation of the aorta and in both common iliac arteries. The sigmoid colon was retracted to the right and the lateral peritoneal fold incised and stripped back exposing the left common, internal, and external iliac arteries. An umbilical tape was placed beneath the common iliac artery to control bleeding, and the common iliac artery was opened by a longitudinal incision. The common iliac artery was compressed from above downward, and the thrombus was milked out of the arterial incision. Suction was applied cephalad and caudad and a few additional clots sucked out. Release of the umbilical tap allowed a brisk stream of blood to flow. The tape was again tightened and the arterial incision closed by a single layer of over-and-over 5-0 nonabsorbable surgical (silk) sutures.

The right iliac vessels were then exposed. The common iliac artery was controlled by an umbilical tape and opened. Large soft clot was milked down from the aortic bifurcation and out the incision in the common iliac artery. After clot extraction a brisk flow of blood was obtained, and the vessel was closed with continuous sutures of 5-0 silk. The abdomen was then closed in layers with interrupted stainless-steel wire sutures. At the termination of the procedure, strong femoral pulses were present bilaterally. The continuous administration of caudal anesthesia, using 0.4% Intracaine, was carried out for 72 hours postoperatively, during which time the feet became progressively warmer and less painful, with restoration of both dorsalis pedis pulses. Intermittently, heparin was given intravenously for 72 hours postoperatively in doses designed to keep the venous coagulation time between 15 and 20 minutes.

The results of both cardiac and vascular surgery were considered excellent on the patient's discharge on Jan. 29, 1952. In a follow-up report in December, 1952, it is stated that this patient is employed in a full-time job with no objective or subjective cardiac or leg symptoms.

## COMMENT

This paper is reported in the hope of clarifying and emphasizing certain important concepts in the management of patients undergoing mitral commissurotomy as regards the possibility or occurrence of peripheral emboli.

It is obvious that if any hope of success is to be entertained in the treatment of postoperative emboli, an awareness of their possibility must be kept in mind and their occurrence immediately detected. Peripheral pulses, including the carotid, axillary, brachial, radial, femoral, popliteal, and dorsalis pedis arteries should be carefully checked preoperatively and recorded. Immediately after commissurotomy and preferably while the patient is still in the operating room, the peripheral pulses should again be checked and recorded. In those patients in whom an embolus is suspected on the basis of the absence of a previously present pulse, skin color, and temperature changes and absent oscillometric pulsations, immediate continuous

sympathetic block to the involved area is instituted. Preparations are made for embolectomy and, if marked improvement, as shown by a return of color, warmth, and vascular pulsation to the extremity, is not noted in one hour, surgical removal of the embolus is performed. Postoperative sympathetic block is maintained for three to five days. Anticoagulant therapy, although used in the case reported, has not been used in the others because of the danger of bleeding from the extensive thoracic and heart wounds. Lumbar sympathectomy has more recently been done in a small series not included in this report.

It is only through early diagnosis and the rapid institution of adequate treatment that lives and limbs will be saved.

In a subsequent report, a critical analysis of the results of treatment in this and other cases will be presented.

SUMMARY

The cause of emboli is discussed.

A case report of the successful removal of an aortic embolus after mitral commissurotomy is presented.

Attention is focused on the importance of a careful and systematic preoperative evaluation of the peripheral vascular system and an immediate postoperative examination of peripheral pulses to detect as soon as possible the occurrence of peripheral emboli.

The principles of management of peripheral emboli following mitral commissurotomy which we have used have been outlined.

# ACUTE PANCREATITIS ASSOCIATED WITH NECROSIS AND PERFORATION OF THE COMMON BILE DUCT

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NOT TOO many years ago it was generally felt that when a diagnosis of acute pancreatitis was suspected, the patient should undergo exploration; if pancreatitis was found, the pancreatic area and the biliary tract were drained. The mortality figures with this form of management were high. When a laboratory procedure for diagnosing acute pancreatitis was devised and found to be reliable, the management of patients with this disease was modified. In most clinics today it is felt that when the diagnosis of acute pancreatitis is made on the basis of elevated serum amylase and/or lipase levels, nonoperative treatment is indicated, except in certain circumstances.[1]

Bockus, Roth, and Sifre [1a] state that the only indications for operation are either "when other acute abdominal emergencies cannot be excluded or if the pancreatitis becomes complicated by suppuration, severe hemorrhage or spreading peritonitis." On the other hand, Rhoads, Howard, and Moss [2] take a diametrically opposed attitude, feeling that all patients with acute pancreatitis should be operated upon whenever possible because of the following considerations:

1. Decompression of the biliary tract reduces the probability of reflex of bile into the pancreatic ducts.
2. Acute biliary tract complications are discovered and treated.
3. Enzyme tests do not differentiate between primary pancreatitis and pancreatitis secondary to inflammation in an adjacent organ.
4. Operation permits the establishment of drainage tracts for necrotic injected enzymes and infected bile.
5. Operation provides a means of later examining the common bile duct roentgenologically.

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2. Rhoads, J. E; Howard, J. M., and Moss, N. H.: Symposium on Recent Advances in Surgical Physiology: Clinical Experiences with Surgical Lesions of the Pancreas, S. Clin. North America **29**:1801 (Dec.) 1949.

With the combined use of operative intervention and peritonitis regime postoperatively, the mortality has declined to 3.2 per cent in the last thirty-one cases.

It is our feeling at the Albert Einstein Medical Center, Northern Division, that conservative treatment is the one of choice, and this has been uniformly practiced ever since it has been possible to make laboratory determinations of the blood enzyme levels. Operation during the acute phase is performed only if we are unable to rule out the presence of other intra-abdominal disease for which we may feel immediate surgery is indicated. Therefore the only patients with acute pancreatitis upon whom operation has been done have been those operated upon for diseases other than the acute pancreatitis.

Within the past few years I have had two patients with acute pancreatitis who had an unusual associated condition for which surgery was definitely indicated. This was necrosis and perforation of the lower portion of the common bile duct, resulting in one case in retroperitoneal extravasation of bile along the right retrocolic gutter and presenting as a mass in the right inguinal area, and in the other case, in bile peritonitis. These two cases are reported in detail since they are so unusual and because the conditions are such as make early surgery imperative.

## REPORT OF A CASE

CASE 1.—W. L., a 53-year-old white man, was admitted to the hospital on Dec. 22, 1949, with the chief complaint that an irreducible mass was present in the right groin for the preceeding 24 hours. The patient stated that he was in his usual health until Dec. 21, when a mass and pain developed in the right groin. Attempts to reduce this mass were unsuccessful. The mass did not appear to increase in size. There was no associated nausea, vomiting, or change in bowel habit. One week before the onset of the present complaint the patient had suffered from "grippe" but had promptly recovered from it. He stated that his asthma, which he had had over 20 years, appeared to be severer and more persistent since the attack of "grippe." The past medical history revealed that the patient had a bilateral herniorrhaphy performed 35 years previously and that he had been suffering from severe asthma for over 20 years.

On physical examination the patient was rather dyspneic and slightly cyanotic. Wheezes could be heard at a distance from the subject. There was intermittent coughing and some expectoration of thick mucoid material. The temperature was 99 F., the pulse rate 100 beats a minute, and the respiratory rate 32 a minute. Examination of the chest revealed no areas of atelectasis or consolidation. The abdomen was soft, slightly distended, and nontender. Normal peristalsis could be heard. In the right inguinal area under the scar of the old herniorrhaphy there was an irregular, moderately firm, irreducible and tender mass.

The leucocyte count was 21,000 cells per cubic millimeter, of which 88% were polymorphonuclear leucocytes, and of these 46% were nonfilamented forms. The erythrocyte count was 5,250,000 cells per cubic millimeter, and the hemoglobin content was 16 gm. per 100 cc.

A diagnosis of a recurrent incarcerated right inguinal hernia was made, and the patient was immediately taken to the operating room.

With the patient under local anesthesia the scar in the right inguinal area was excised and the deeper tissues incised. When Scarpa's fascia was reached, it was observed that the tissues were bile stained and edematous. After a retroperitoneal plane was broken through, bile poured forth. No hernia was found. A drain was placed in the incision, and the patient was put to sleep with cyclopropane, ether, and oxygen anesthesia. A midrectus incision was made, and the peritoneal cavity was entered. No free bile was seen. Numerous areas of fat necrosis were scattered over the greater omentum. The tissues behind the cecum and ascending colon were bile stained. It was apparent that there was some perforation of the biliary tract, with extravasation of bile retroperitoneally along the right colic gutter into the groin. The abdominal

incision was extended into the upper abdomen. The structures of the entire lesser omental bursa were obscured by fat necrosis and edema. There were numerous stones in the gall bladder. It was presumed that the perforation was probably in the pancreatic portion of the common bile duct, since perforation above this point would result in extravasation of bile into the peritoneal cavity. Therefore the gall bladder was opened, numerous stones removed, and a large tube placed in the gall-bladder lumen, in the hope that this would act as a shunt and prevent further leakage of bile into the retroperitoneal structures. The abdominal incision was closed in layers and reinforced by through-and-through sutures of heavy Dermalon.

Treatment in the postoperative period consisted of administration of penicillin procaine for aqueous injection (Crysticillin) and streptomycin, and of frequent blood transfusions, intravenous injections of vitamins, continuous gastric suction, and continuous intranasal oxygen.

On the second postoperative day, bile started to drain from the cholecystostomy tube and there was no longer any drainage from the inguinal wound. Atelectasis of the right lower lobe developed, and it was necessary on two occasions to clear the tracheobronchial tree by bronchoscopic aspiration. Repeated intercostal blocks were done to make breathing easier. Morphine was omitted, since it was felt to be contraindicated in a patient with severe asthma and especially in the presence of pancreatitis. The abdomen remained soft and slightly distended during the entire postoperative course. Peristalsis was audible from the second postoperative day until the time of death, on Dec. 25.

The pulse rate during the postoperative course varied from 104 to 140 beats a minute. The temperature, only 100 F. rectally, for the first two postoperative days, gradually rose to 104 F. rectally at the time of death. The respiratory rate was persistently beween 28 and 40 per minute.

The serum amylase and lipase levels the morning after operation were reported as 300 and 0.4 units, respectively. The blood urea nitrogen on Dec. 23 was 25 mg. and the serum bilirubin, 1.9 mg. per 100 cc. A urinalysis done 12 hours after operation was positive for bile, negative for urobilinogen, and showed some albumin. Several blood sugar and serum calcium determinations done during the postoperative course were normal. All studies repeated on the day of death showed no significant change from the initial levels.

Autopsy was performed 18 hours after death. In addition to the extensive fat necrosis in the abdomen, the only other interesting finding was the total necrosis of the pancreas together with the intrapancreatic portion of the common bile duct. It was impossible to identify any structure resembling a common bile duct in that portion of its course. No stone was found impacted at the papilla of Vater.

*Comment.*—Although other cases of acute pancreatitis with necrosis of most or all of the pancreas have been reported, this is apparently the first case in which there was total necrosis of the intrapancreatic portion of the common bile duct with extravasation of bile along the right retrocolic gutter into the right groin. It is interesting to note that when the cholecystostomy tube started to drain bile, the drainage from the groin ceased. However, the decompression of the biliary tract did not arrest the severity of the pancreatitis, and the patient's course was progressively downhill. Although the disease was probably in progress for several days before the patient was first seen, he did not appear acutely ill. This case demonstrates how the severity of the pancreatitis is not necessarily correlated with the clinical picture. The amylase and lipase levels were low, probably the result of the extensive destruction of the pancreas. The relation between pancreatic and pulmonary disease has been commented upon on numerous occasions in the literature.

Case 2.—E. A., a 71-year-old white woman, was admitted to the hospital on Dec. 14, 1952. The patient had been well until Dec. 13, when lower abdominal cramps and vague periumbilical discomfort developed. Soon after the onset of these complaints she vomited. The vomiting did not persist. The patient had three normal bowel movements the day of the onset of the complaints, but none the following day. She had passed no flatus for 18 hours before admission to the hospital. There had been no attacks of pain in the past history similar to

that in the present. The patient had just recovered from a "virus infection with cough" which had been present for about two weeks. The patient had a "mild cardiac" condition and had been given a salt restriction and mercurial diuretic regimen.

The patient walked into the hospital and did not appear to be acutely ill. The temperature was 101 F., the pulse rate 78 beats a minute, and the respiratory rate 20 a minute. Examination of the chest revealed some suppression of the breath sounds and crepitant rales at the right base. No abnormal sounds were heard upon auscultation of the heart. The abdomen was slightly distended. No peristalsis could be heard. There were definite deep tenderness and guarding of the entire lower and right upper abdomen. The leucocyte count was 15,500 cells per cubic millimeter, of which 92% were polymorphonuclear leucocytes; of these, 33% were nonfilamented forms. The erythrocyte count and hemoglobin content were normal. Urinalysis showed nothing abnormal. A flat x-ray film of the abdomen showed a few loops of small intestine containing gas, but these did not appear to be unduly distended. In addition, there were air and fluid under the right diaphragm, indicating to the roentgenologist that an active process was present in this area. X-rays of the chest revealed the presence of some free fluid in the right costophrenic sulcus. The serum amylase level was reported as 780 units. In view of all the findings mentioned, it was felt advisable to operate rather than to follow a conservative regimen.

The patient was taken to the operating room and with use of general anesthesia, a right midrectus incision was made. When the peritoneal cavity was entered, a large amount of free bile was encountered. This was aspirated and a culture taken. A few areas of fat necrosis in the greater and lesser omenta were apparent. Except for some congestion the gall bladder appeared normal, and on palpation no stones could be felt. Whenever the gall bladder was squeezed, bile could be seen pouring out from the foramen of Winslow. Careful dissection in this area revealed that there was a perforation in the common bile duct just as it entered into the pancreas All the structures of the lesser omental bursa were edematous. A No. 14 French T-tube was placed into the perforation of the common bile duct. A sump drain was placed down to the foramen of Winslow and allowed to come out through a stab wound to the right of the incision, together with the T-tube. The abdomen was closed in layers and reinforced by through-and-through sutures of heavy Dermalon.

The postoperative course was entirely uneventful. The pulse rate never exceeded 76 beats a minute. The temperature on only one occasion rose to 100 F. A chest x-ray done on Dec 16 revealed that there was more fluid in the right hemithorax. It was felt this was the result of infradiaphragmatic irritation. The culture of the bile aspirated at operation was reported as sterile. The pancreatitis regimen, as described in Case 1, was adopted. Peristalsis became active on the third postoperative day. The patient was permitted to eat on the fifth postoperative day. The serum amylase level fell to 160 units on Dec. 18. The serum lipase level fell from 2.5 units on the day of admission to 1 unit on Dec. 18. X-rays of the upper gastrointestinal tract taken on the eighth postoperative day revealed no abnormalities. A cholangiogram done on Dec. 25 revealed the common duct to be dilated; dye readily passed into the duodenum; no stones could be seen in either the common bile duct or the gall bladder; there was reflux of bile into the pancreatic duct. The patient was discharged from the hospital on Dec. 28, 1952. A chloangiogram repeated on Feb. 14, 1953, showed no appreciable change.

*Comment.*—This patient did not look very ill when first admitted to the hospital. The presence of the leucocytosis and the roentgenologist's finding of fluid and air under the diaphragm indicated that exploratory laparotomy was necessary. However, bile peritonitis was not expected. On several occasions in the past it has been observed by others at the hospital, as well as by myself, that bile in the peritoneal cavity in the aged patient has been associated with very little local or systemic reaction. The exact sequence of the pathologic changes in this case is still uncertain —whether there was a primary perforation of the common bile duct secondarily producing a pancreatitis or whether the pancreatitis preceded the perforation. The absence of calculi on cholangiography in either the common duct or the gall bladder makes the latter more likely. It is quite possible that had a serum amylase deter-

mination been made prior to the time of admission that it might have been higher. The completely negative report by the roentgenologist of the x-ray of the upper gastrointestinal tract rules out any gastric or duodenal disease as being a causative factor.

## COMMENT

To my knowledge perforation of the common bile duct as reported in these two cases has not previously been reported. Perforation, when it does occur, is secondary to diverticula of the duct, to calculi eroding through the wall, to perforation of a duodenal ulcer in the vicinity of the duct involving the duct in an erosive manner, or to trauma.

At this hospital, whenever surgery is performed in a patient with acute pancreatitis, it is done either because the true diagnosis is not suspected or because other associated diseases or complications make surgery urgent during the acute phase. As has been previously mentioned, it is our feeling that if the diagnosis of pancreatitis can be proved, nonoperative treatment is indicated. We have seen conditions other than acute pancreatitis produce elevated levels of serum amylase. These have included free perforations of duodenal ulcer, ulcers perforating posteriorly into the pancreas, renal disease, mumps, carcinoma of the head of the pancreas, trauma, and, on occasion, severe shock states, such as those associated with extensive myocardial infarction. The administration of morphine or morphine-like drugs may also produce elevated serum amylase levels. The levels in these circumstances have rarely been over 1,000 units. Whenever a patient with acute abdominal disease is admitted to our hospital and pancreatitis is suspected, in addition to serum amylase and lipase determinations an x-ray of the abdomen is done in order to rule out a free perforation of a viscus. If such a perforation can be ruled out and the serum amylase level is greater than 1,000 units, we adopt a conservative regimen consisting of continuous gastric suction, bed rest, antibiotics, intravenous fluids, administration of drugs such as atrophine and methantheline (Banthine) bromide, sedation, and, more recently, splanchnic block to relieve pain. When we cannot rule out other associated disease, exploration is done. We also feel that while hemorrhage and necrotic pancreatitis are more extensive and progressive stages of the so-called edematous type, surgery aimed at side-tracking the bile and relieving tension upon the gland by incising the peritoneum over it will not arrest the course of the disease.

The only argument offered by the proponents for early operation which seems valid is the one which states that other conditions may be overlooked. However, if a high index of suspicion is exercised and intensive study is done to rule out other lesions or complications which may necessitate operation, then this argument can be overruled.

## SUMMARY

Operation was carried out in two patients who had perforation of the common bile duct associated with acute pancreatitis.

The indications for operation in acute pancreatitis are discussed.

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# HEMORRHAGIC ASCITES AND HEMOTHORAX ASSOCIATED WITH BENIGN PANCREATIC DISEASE

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ST. LOUIS

IN PANCREATIC diseases the presence of bloody fluid in the peritoneal and pleural cavities is usually indicative of hemorrhagic pancreatitis or carcinoma of the pancreas with metastases. There are numerous reports in the literature of hemorrhagic ascites in hemorrhagic pancreatitis [1]; however, thorough search of the literature revealed no reported cases of hemorrhagic ascites associated with chronic pancreatitis and pseudocysts of the pancreas. Werner [2] reported a case of hemothorax associated with chronic recurring pancreatitis. The two cases reported herein are unusual in that they were associated with neither hemorrhagic pancreatitis nor carcinoma.

## REPORT OF CASES

CASE 1.—A. L., a Negro woman aged 30, came under my observation on Aug. 12, 1952, complaining of nausea, vomiting, diarrhea, severe upper abdominal pain, moderate abdominal enlargement, and a weight loss of approximately 25 lb. (11.3 kg.).

*Past History.*— Five months prior to this admittance she was hospitalized on the gynecological service with symptoms of nausea, vomiting, and moderate generalized abdominal pain. She was given antibiotics and other supportive measures based on a clinical impression of pelvic inflammatory disease. In view of the upper abdominal manifestations, upper gastrointestinal series were obtained, and the roentgenological diagnosis was gastric ulcer. She was transferred to the medical service for therapy but signed out of the hospital shortly afterward.

*Physical Examination.*—The patient showed evidence of marked weight loss. The blood pressure was 90/60, temperature 98.6 F., pulse rate 96, and respirations 20. There was dullness to percussion in both lung bases posteriorly and laterally on the left side, with diminished breath sounds in both bases. Abdominal examination revealed abdominal distention. No other positive findings were noted.

*Laboratory Studies.*—Examination of the urine was essentially noncontributory. Blood studies showed moderate lymphocytosis. Blood chemistry revealed that the nonprotein nitrogen, calcium, and amylase values were within normal limits. The total value for serum protein was 5.3 gm. per 100 cc. (albumin 2.5 gm. and globulin 2.8 gm.). The albumin-globulin ratio was 1 : 1.

*Clinical Course.*—Paracentesis abdominis was performed several times, but on each occasion only about 2,000 cc. of sanguineous fluid could be obtained. This fluid had a specific gravity of 1,014 and on microscopic examination showed only crenated red blood cells. However, it was not examined for diastase content. Histological sections showed no evidence of malignant growth. On Sept. 5, the upper gastroinestinal series was repeated, and findings were interpreted as gastric carcinoma (Fig. 1).

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From the Department of Surgery, Homer G. Phillips Hospital.

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Despite the negative histological findings a diagnosis of carcinoma was made on the basis of the hemorrhagic ascites and roentgenological interpretation, and the patient was sent home to die.

However, the patient did not die; indeed, after approximately three weeks her general condition improved, as shown by a gain in weight, improved appetite, and no recurrence of ascites. Gastroscopy revealed what was interpreted as either an extraluminal mass or an intramural carcinoma presumably causing the defect as noted in Figure 1. A biopsy specimen taken from the stomach wall at gastroscopy was reported as normal. Repeat abdominal films (Fig. 2) revealed a calcareous pancreas. On Oct. 25, an exploratory laparotomy revealed approximately 1,500 cc. of serosanguineous fluid which had a diastase value of 450 Somogyi units and a few scattered areas of fat necrosis which histologically showed only evidence of fibrosis.

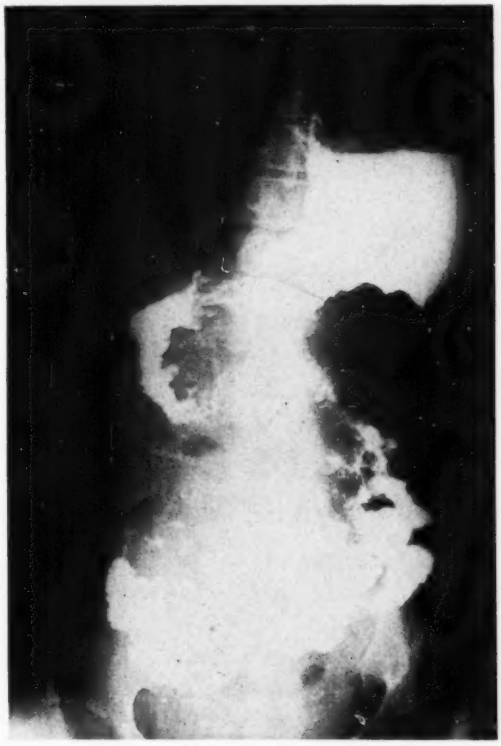

Fig. 1.—Roentgenogram of upper gastrointestinal tract showing a large irregular filling defect which involves the pars media and pyloric region, giving impression of malignant growth.

Numerous fibroserous adhesions were noted between the liver, stomach, colon and peritoneum. The greater curvature of the stomach was adherent to the anterior parietal peritoneum and the surrounding viscera. The pancreas was moderately enlarged and firm. Other organs in the abdominal cavity were not unusual. The postoperative course was uneventful, and the patient was discharged asymptomatic on Nov. 8, 1952. She returned for monthly follow-up visits, and during the last four months there has been a gradual gain in weight with no recurrence of ascites or abdominal pain.

CASE 2.—H. R., a Negro man aged 44, entered the hospital on Sept. 4, 1952, complaining of moderate generalized abdominal pain, abdominal distention, anorexia, and gradual weight loss.

*Past History.*—The patient had a previous hospital admission three and one-half years earlier, and on the basis of an alcoholic history and other findings a diagnosis of alcoholic

cirrhosis with ascites was made. Paracentesis abdominis yielded 3,000 cc. of straw-colored fluid. No bacteriological analysis of fluid was made at that time. X-rays of the chest during this admission revealed a small right pleural effusion.

Two and one-half years prior to the present admission he entered the hospital complaining of abdominal pain of six days' duration, which began in the left upper quadrant with radiation to epigastrium and left chest, associated with nausea and vomiting. The diagnosis of pancreatitis was substantiated by serum and urinary amylase values of 500 and 6,000 Somogyi units, respectively. Abdominal examination revealed a cystic mass measuring approximately 6 by 3.5 in. (15.2 by 3.8 cm.) which was thought to be a pancreatic cyst. At operation a cyst of the pancreas was found and marsupialized.

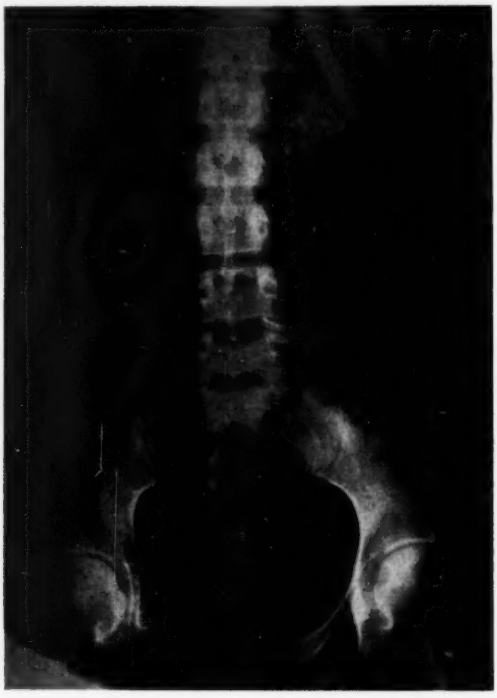

Fig. 2.—Roentgenogram showing irregular area of amorphous calcification approximately 8 cm. in diameter in midlumbar region, giving impression of calcified pancreatic tumor.

The diastase content of the cyst fluid was 1,875 and 3,100 Somogyi units, and histological sections of the cyst wall showed no sign of malignant growth. One week after the operation the serum amylase was 250 Somogyi units, and the patient was discharged asymptomatic three weeks later.

*Physical Examination.*—On examination the patient's temperature was 98 F., pulse rate 72, respirations 28, and blood pressure 130/62. The only significant finding was marked abdominal distention.

*Laboratory Studies.*—Laboratory studies revealed traces of sugar on several occasions but were otherwise essentially negative. Blood chemistry showed serum calcium levels of 11 mg. and 10 mg. per 100 cc. on several occasions.

*Clinical Course.*—On Sept 7, abdominal paracentesis yielded 7,000 cc. of coffee-ground fluid which showed no evidence of malignant growth. On Sept. 15, an upper gastrointestinal series

was started in order to substantiate what was thought to be a recurrence of the pancreatic cyst; however, signs of partial intestinal obstruction developed about eight hours after barium meal. After several days of conservative therapy all of the signs subsided.

Shortly afterward physical findings and x-rays (Fig. 3) suggested a right hydrothorax, and thoracentesis revealed 1,000 cc. of hemorrhagic fluid. Serum amylase at this time was 1,500 Somogyi units. The patient was transferred to the surgical division, and on two occasions thoracentesis was repeated and yielded 1,800 cc. and 950 cc. of hemorrhagic fluid, respectively. Abdominal paracentesis was also performed and 3,950 cc. of hemorrhagic fluid was obtained which had a specific gravity of 1.012, did not clot, and showed crenated red blood cells and lymphocytes.

Fig. 3.—Roentgenogram of chest showing an opacity involving greater portion of right chest. Only a small area of aerated lung is seen in mediastinal portion of upper one-third of chest. Impression is of large pleural effusion.

Histological sections of this fluid showed no evidence of malignant growth, but the diastase value was 23,000. Serum diastase was 2,300 Somogyi units at this time. For approximately one month the patient was treated symptomatically.

At this time x-rays of the chest showed complete resorption of the fluid. However, because of increasing abdominal distention, he was operated upon, and celiotomy revealed 3,800 cc. of hemorrhagic fluid which proved later to have a diastase value of 6,850 Somogyi units. Numerous fibrinous adhesions were noted between the viscera and the site of the previous operation.

A cystic mass approximately 10 by 8 cm. was palpated behind the stomach. During the operation the duodenum was inadvertently entered; the opening was repaired immediately. The postoperative course was uneventful, and approximately two weeks later the patient was discharged from the hospital. Reevaluation on several follow-up visits revealed no evidence of abdominal distention. There was a gain in weight. Chest x-rays revealed nothing abnormal.

## COMMENT

It has been observed on numerous occasions that in acute pancreatitis the peritoneal fluid, ranging up to several hundred centimeters in quantity, is an exudate which is usually clear but may contain hemolyzed or nonhemolyzed red blood cells.[3] In addition, pleural effusion consisting of a serous-like fluid may be noted.[4] Grossly bloody fluid, however, is unusual in pancreatitis without necrosis and hemorrhage.

## SUMMARY

Two cases of hemorrhagic ascites associated with chronic calcareous pancreatitis and one case of recurrent pancreatic cyst are reported. An associated hemothorax was present in one instance.

2601 N. Whittier St.

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# POSTOPERATIVE LOSS OF SUGAR IN URINE FOLLOWING INTRAVENOUS INFUSION OF FRUCTOSE (LEVULOSE)

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AND
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IN A PREVIOUS report [1] the urinary losses of sugar following the intravenous infusion of fructose (levulose) and of D-glucose (dextrose) were compared in an unselected group of patients. In the present study a similar comparison was made in patients during the immediate postoperative period. No other observations have been reported thus far on the behavior of fructose given by intravenous infusion after operation.

## METHODS

Observations were made in two groups of patients. In the first group there were 10 patients all well nourished and undergoing various major surgical procedures under general anesthesia. During each of the first four postoperative days, 2 liters of 10% sugar was infused, using on alternate days 10% fructose [2] and 10% dextrose. On the first day, six patients were given dextrose and four fructose. An attempt was made to give each infusion at the same rate, but in each case the duration was measured and recorded.

In the second group were patients having similar operative procedures but receiving only fructose or fructose and protein hydrolyzate (Amigen). In eight patients observed for 28 postoperative days the daily intake consisted of 10% fructose alone given at a rate of about three hours for each liter. In 21 patients observed for 34 postoperative days, the daily intake consisted of 3 liters, 2 containing 10% fructose (each given in 90 minutes) and 1 containing 5% fructose and 5% protein hydrolyzate (given in 3 hours).

In all cases 24-hour urine collections were measured and analyzed for total reducing substances by the method of Nelson.[3]

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Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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3. Nelson, N.: A Photometric Adaptation of the Somogyi Method for the Determination of Glucose, J. Biol. Chem. **153**:375, 1944.

FINDINGS AND COMMENT

The findings are shown in Tables 1 and 2. It will be noted in Table 1 that when the two infusions were given on alternate days, the output of sugar with fructose was lower than the output with dextrose. This was evident in calculating the totals for the entire postoperative period in all cases, the mean two-day values being 19.7 gm. for fructose, 50.6 gm. for glucose. Analysis of these data showed a minimum difference of 40.2 gm. for fructose, 56.4 gm. for glucose; a maximum difference of 3.1 gm. for fructose, 24.8 gm. for glucose. Study of each individual day showed little difference in output on the first postoperative day (day of operation), a mean of 12.0 gm. for fructose as compared with 14.5 gm. for glucose. This similarity is partly due to the effect of anesthesia on the metabolism of fructose, which behaves somewhat like glucose under these conditions,[4] partly to the fact that fructose was inadvertently given more rapidly; i. e., scrutiny of Table 1 shows that all but one of the six fructose infusions given on the first postoperative day were more rapid (three, four, four, four, and five hours), wheras the dextrose infusions each lasted six hours. During the second, third, and fourth postoperative days the differences between fructose and glucose output were striking—a mean daily output of 12.2, 8.8, and 7.2 gm. of fructose, as compared with 30.3, 19.1, and 32.1 gm. of glucose, respectively. Scrutiny of the duration of the infusions shows fairly consistent uniformity.

In Table 2 are listed the range of output and the mean in the patients given only fructose with or without amino acids (protein hydrolyzate). In the group of 28 postoperative 24-hour periods during which fructose alone (200 gm.) was given, the mean loss of sugar was 7.9 gm.; in the group of 34 postoperative days during which fructose (250 gms.) and protein hydrolyzate (50 gm.) were given, the mean loss was 8.9 gm. This is to be compared with previous observations in which dextrose alone (200 gm.) given at a similar or slower rate was followed by a loss of 26.2 gm.—a statistically significant difference.

The present findings indicate that during the postoperative period fructose may be infused at faster rates than dextrose with less spillage of sugar in the urine. Though blood levels were not measured, previous observations [1] have shown that lower values are found with fructose than with dextrose. High blood levels tend to produce intracellular dehydration and glucosuria. Since diuresis is a usual accompaniment of glycosuria, it is probable that the loss of water is less pronounced with fructose than with dextrose, at least during the period of infusion, even though the total 24-hour output showed no difference.

Clinical observation revealed no differences in the behavior of the patients whether they were given dextrose or fructose. The incidence of phlebitis was low with both sugars, and no difference could be detected between them. Nitrogen excretion studies were made in several cases, listed in Table 1, and found to be the same with dextrose as with fructose.

Attention should be called to the wide variations in the degree of postoperative glycosuria from patient to patient. A few, even when given dextrose fairly rapidly, spill relatively little sugar, whereas others spill a good deal at similar rates. This

4. Weichselbaum, T. E.; Margraf, H. W., and Elman, E.: The Metabolism of Intravenously Infused Fructose in Man, Metabolism, to be published.

TABLE 1.—*Total Reducing Bodies in Urine* *

| Case | Age, Yr. | Sex | Operation | Postoperative Days 1 Fructose | 1 Glucose | 2 Fructose | 2 Glucose | 3 Fructose | 3 Glucose | 4 Fructose | 4 Glucose | Totals (2 Days) Fructose | Totals (2 Days) Glucose |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 44 | M | Gastrectomy | 2.4 (5) | ..... | ..... | 0.7 (6) | 7.0 (5) | ..... | ..... | 24.1 (5) | 9.4 | 24.8 |
| 2 | 59 | F | Cholecystectomy | 12.8 (4) | ..... | ..... | 32.4 (5) | 6.3 (5) | ..... | ..... | 27.4 (6) | 19.1 | 59.8 |
| 3 | 24 | F | Cholecystectomy | 12.3 (3) | ..... | ..... | 59.4 (4) | 18.5 (5) | ..... | ..... | 43.0 (4) | 30.8 | 102.4 |
| 4 | 68 | F | Abdominoperineal resection | 8.1 (10) | ..... | ..... | 34.7 (6) | 3.7 (8) | ..... | ..... | 33.0 (9) | 11.8 | 67.7 |
| 5 | 30 | M | Closure duodenal ulcer | 9.2 (4) | ..... | ..... | 29.0 (6) | ..... | (37.0) (4) † | ..... | ..... | .... | .... |
| 6 | 56 | M | Gastrectomy | 27.4 (4) | ..... | ..... | 25.4 (6) | ..... | 31.0 (7) | 12.8 (4) | ..... | 40.2 | 56.4 |
| 7 | 35 | M | Abdominoperineal resection | ..... | 11.0 (6) | 11.9 (6) | ..... | ..... | 16.8 (5) | 1.1 (6) | ..... | 13.0 | 27.8 |
| 8 | 58 | F | Colectomy | ..... | 23.0 (6) | 7.1 (7) | ..... | ..... | 14.1 (7) | 7.6 (5) | ..... | 14.7 | 37.1 |
| 9 | 66 | M | Abdominoperineal resection | ..... | 6.2 (6) | 11.1 (3) | ..... | ..... | 22.4 (4) | 7.5 (3) | ..... | 18.6 | 28.6 |
| 10 | 34 | M | Gastrectomy | ..... | 17.7 (6) | 18.9 (8) | ..... | ..... | 11.0 | ..... | ..... | .... | .... |
| | Mean: | | fructose..... | 12.0 | | 12.2 | | 8.8 | | 7.2 | | 19.7 | |
| | Mean: | | glucose..... | | 14.5 | | 30.3 | | 19.1 | | 32.1 | | 50.6 |

* Measured in grams per 24 hours while patient is given 2 liters of 10% dextrose or fructose, each given on alternate days. Numbers in parentheses refer to duration (in hours) of the total 2 liter infusions.

† Two liters of invert sugar given on this day were not included in calculating totals or means.

difference is probably due to individual variations in the homeostatic mechanisms which occur after trauma, i. e., in the intensity of the "stress" reaction. For this reason, experiments in the first group (Table 1) tend to have greater validity, inasmuch as each patient served as his own control. For example, in Case 1 the patient obviously possessed considerable ability to retain glucose since there was very little spillage (0.7 gm.) on the second postoperative day and only 24.1 gm. on the fourth day. On the other hand, in Case 3 the patient on comparable days spilled a great deal of sugar (59 and 43 gm., respectively). Had patients similar to the patient in Case 1 been compared, it is clear that less difference would have been observed in the glycosuria after either sugar was given than with patients similar to the third patient. Similar differences were noted in patients given only one sugar during the entire postoperative period, as shown by the range of excretion with both fructose and dextrose, e. g., from 1.5 to 88 gm. per 24 hours. Here statistical analysis revealed a marked and significant difference between the amount of sugar lost when dextrose was given, as compared with fructose, indicating that the means as recorded were valid.

TABLE 2.—*Postoperative Urinary Sugar Losses*

| | No. Postoperative Specimens | Average, Gm./24 Hr. | Range, Gm./24 Hr. |
|---|---|---|---|
| Glucose * (2 L. 10%/day) | 76 | 26.2 | ..... |
| In water | 40 | 18.3 | 1.5-88 |
| In saline | 36 | 34.1 | 6.1-82 |
| Fructose (2 L. 10%/day) | 28 | 7.9 | 1.0-31.2 |
| Fructose and protein hydrolyzate (2 L. 10% fructose, 1 L. 5% fructose and 5% protein hydrolyzate/day) | 34 | 8.9 | 0.7-57.0 † |

* Data from previous studies partly reported (Ann. Surg. **130**: 703, 1949).
† Only one specimen contained 57 gm.; the next highest contained 23.7 gm.

The present findings are also of interest in view of the well-known loss of glucose tolerance after operation. It seems clear that there is no similar loss of fructose tolerance.

## SUMMARY AND CONCLUSIONS

Infusions on alternate days of 2 liters of 10% fructose during four postoperative days in 10 patients revealed an average loss of sugar nearly three times greater with dextrose than with fructose. The difference on the first postoperative day was insignificant, but on the fourth day was nearer five times greater with dextrose than with fructose.

In eight patients given 2 liters of 10% fructose per day during 28 postoperative days, the mean daily loss of sugar in the urine was 7.9 gm.; in 21 patients given 3 liters containing fructose (250 gm.) and protein hydrolyzate (Amigen, 50 gm.) during 34 postoperative days, the mean daily loss of sugar was 8.9 gm. This is one-third the loss noted with a control group in which following the infusion of 2 liters of 10% dextrose (200 gm.) given at a similar or slower rate the comparable figure was 26.2 gm.

It is concluded that 10% fructose given at a rate of two to three hours per liter in adult patients during the postoperative period is followed by a much smaller loss of urinary sugar than 10% dextrose.

# SMALL BOWEL OBSTRUCTION

## A Complication of Combined Abdominoperineal Excision of the Rectum

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POSTOPERATIVE mechanical small bowel obstruction following abdominoperineal resection of the rectum is a relatively frequent and often fatal complication. Twenty-eight per cent of the postoperative deaths in the present series were a direct result of this complication, and considerable morbidity resulted from obstruction in those patients who recovered.

### MATERIAL

Records of 214 consecutive one-stage abdominoperineal resections performed at The Ellis Fischel State Cancer Hospital from May, 1940, to May, 1952, were studied. Ninety-two patients were females, and 122 were males. There were 14 postoperative deaths, a mortality rate of 6.5%. There were eight anatomically proved postoperative small bowel obstructions, and two fatal cases in which the diagnosis was based on clinical grounds. In these 10 cases, there were four deaths. In reviewing the records, it would be difficult to determine the actual number of true mechanical obstructions in which recovery occurred on conservative treatment; accordingly, only the above cases were considered for study. The actual incidence of this complication is no doubt greater than is indicated.

### ANALYSIS

*Time Interval.*—Most of the obstructions occurred early: five of them between the third and fifth postoperative day; the remainder at 12, 15, 26, and 28 days. One occurred almost five months postoperatively.

*Site of Obstruction.*—The terminal ileum was obstructed in all cases by adhesions to the pelvic floor as the most common site of attachment (in 8 cases out of 10). Two obstructions were caused by small bowel trapped between the colostomy and the lateral abdominal wall. In six cases there was kinking of the small bowel adherent in this region, producing the obstruction. In all the cases of obstruction the pelvic floor had been closed at the time of surgery. From review of the records, it is impossible to ascertain whether or not the peritoneal floor had disrupted to cause the obstruction. As noted below, no obstruction occurred in the 12 cases in which the pelvic floor was left open.

*Variation in Technique.*—There were 69 left lower quadrant colostomies, in all of which the gutter was closed at the time of operation. One postoperative obstruc-

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tion in this group developed from a knuckle of bowel working its way between the colostomy and the lateral abdominal wall. The other obstruction of a similar nature occurred in 1 of the 144 central colostomies, and in this instance no attempt had been made at the time of surgery to close the gutter. However, closure of the gutter in the central colostomies was done in only four cases, so that failure to close the gutter was of no significance. In 12 cases the floor was not reperitonealized, and in none of these did postoperative obstruction develop from pelvic floor adhesions.

*Sex.*—Of those patients with pelvic floor obstruction, four were males and two females. Eighteen of the 92 women also had removal of contiguous pelvic organs, and one of the pelvic floor obstructions occurred in this group.

## COMMENT

The incidence and locations of postoperative small bowel obstruction in this series correspond generally with those in other reports.[1] The site of the colostomy, whether left lower quadrant or central, seems to be unimportant. However, if the gutter is small, as in a left lower quadrant colostomy, it should be closed. The surgeon's opinion as to the adequacy of reperitonealization in those cases in which pelvic floor obstructions subsequently developed could not be determined accurately from the records. It is of interest, however, that in the 12 cases in which no reperitonealization was attempted, no obstruction resulted from subsequent pelvic floor adhesions. This suggests that if there is any question as to the adequacy of the reperitonealization of the pelvic floor this structure should not be reperitonealized.

## SUMMARY AND CONCLUSIONS

In a series of 214 consecutive one-stage abdominoperitoneal resections there were 10 instances of postoperative small bowel obstruction. Among these there were 4 deaths, representing 28% of the total of 14 postoperative deaths, a mortality rate of 6.5%.

The obstruction was found and relieved at a second operation in 8 of the 10 cases of postoperative obstructions, with six survivals.

The most common site of postoperative intestinal obstruction was in the floor of the pelvis, in all of which reperitonealization was carried out.

Since no obstruction occurred in 12 cases in which the pelvis was left open, it is inferred that in cases in which reperitonealization is unsatisfactory or dubious the procedure should not be done.

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1. Ulfelder, H., and Quinby, W. C., Jr.: Small Bowel Obstruction Following Combined Abdominoperineal Resection of the Rectum, Surgery **30**:174-177, 1951. Goligher, J. C.; Lloyd-Davis, O. V., and Robertson, C. T.: Small-Gut Obstructions Following Combined Excision of the Rectum, with Special Reference to Strangulation Round the Colostomy, Brit. J. Surg. **38**:467-473, 1951.

# CARCINOMA OF THE STOMACH FOLLOWING GASTROENTEROSTOMY FOR DUODENAL ULCER

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AND
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LOS ANGELES

IN CONTRAST to the infrequent coexistence of duodenal ulcer and gastric carcinoma, the incidence of gastric carcinoma is high in gastric lesions which occasionally develop in patients after gastroenterostomy has been performed for treatment of duodenal ulcer.

In view of this high incidence, it is surprising that so few reports dealing with such lesions have appeared. In 1932 Wilbur and Rivers [1] reported on 33 patients in whom duodenal ulcer was associated with gastric carcinoma. Four of these patients had previously been subjected to gastrojejunostomy. Fischer, Clagett, and McDonald,[2] in 1947, reported 48 cases of duodenal ulcer coexistent with gastric carcinoma. Gray and Lofgren [3] found gastric neoplasm in 27% of 41 patients in whom gastric lesions developed after gastroenterostomy. Two similar cases were reported by Epstein and Mendell in 1950.[4]

Three such cases have been encountered in our institution during a three-year period. Because of the paucity of information on the subject and because of the more frequent use of gastroenterostomy in association with vagotomy for the treatment of duodenal ulcer, a discussion of this problem seems indicated.

## REPORT OF CASES

CASE 1.—R. R., a 61-year-old white man, was admitted to the hospital in May, 1949, with a history of postprandial epigastric pain which had been present for a year previous to admission. Temporary relief had been obtained by conservative therapy which consisted of bland diet, antispasmodics, and antacids. Four weeks prior to admission the pain became severer, and a mod-

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Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

1. Wilbur, D. L., and Rivers, A. B.: Association of Duodenal Ulcer and Gastric Carcinoma, Proc. Staff. Meet., Mayo Clin. **7**:241-243, 1932.

2. Fischer, A.; Clagett, O. T., and McDonald, J. R.: Coexistent Duodenal Ulcer and Gastric Malignancy, Surgery **21**:168-174, 1947.

3. Gray, H. K., and Lofgren, Karl A.: The Significance of an Ulcerating Lesion in the Stomach Following Gastroenterostomy, Surg., Gynec. & Obst. **89**:285-291, 1949.

4. Epstein, H. J., and Mendell, T. H.: Co-Existence of Duodenal Ulcer with Independent Gastric Carcinoma, Gastroenterology **16**:602-608, 1950.

erate degree of abdominal distention developed. The patient had been admitted to this hospital in 1928 for the treatment of similar gastrointestinal symptoms. At that time, gastric acidity values of 40 degrees free hydrochloric acid, with a total of 65 degrees, were obtained. Roentgenograms had demonstrated an active duodenal ulcer, and a gastroenterostomy was performed.

Physical examination performed at the time of the present admission revealed nothing abnormal except for slight epigastric tenderness and a moderate abdominal distention.

The hemoglobin content was 15 gm. per 100 cc., and stool examination for occult blood was negative. Gastric analysis revealed 35 degrees free hydrochloric acid, with a total of 59 degrees.

Roentgenograms demonstrated a marked deformity and narrowing of the antrum, interpreted as "gastric ulcer" (Fig. 1). A persistent deformity of the duodenal bulb was observed, and retention of 60% was present after six hours. A diagnosis of gastric ulcer and dysfunction of the gastroenteric stoma was made.

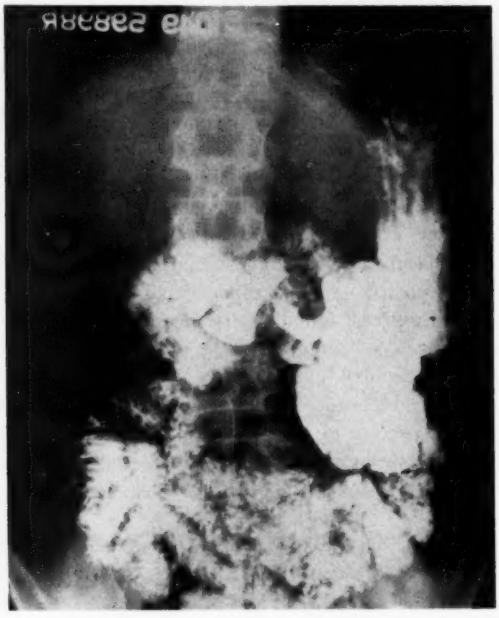

Fig. 1 (Case 1).—Roentgenogram demonstrating a deformity of the antrum of the stomach and first portion of the duodenum, interpreted as probable gastric ulcer. A large carcinoma involving the antrum was found at operation.

At operation a large neoplasm extending into the regional lymph nodes was found on the lesser curvature of the stomach. Microscopic sections revealed an ulcerating scirrhous carcinoma of the stomach with metastases to the regional lymph nodes.

Case 2.—E. P., a 64-year-old white man, was admitted to the hospital in June, 1951, with a five-month history of increasing epigastric pain associated with weakness, intermittent melena, occasional vomiting, and a weight loss of 11 lb. (5 kg.). The severity of the symptoms had increased despite treatment with antispasmodics, antacids, and bland diet.

In 1923 this patient had undergone gastroenterostomy for duodenal ulcer. After this procedure he had remained asymptomatic until the onset of his present illness.

On admission to the hospital in June, 1951, the physical examination was negative except for slight tenderness in the epigastrium. The hemoglobin level was 14.2 gm. per 100 cc., and stool examination for occult blood was negative. Roentgenograms revealed a partial pyloric "obstruction" without evidence of marginal ulcer. There was a persistent deformity of the duodenal bulb

Fig. 2 (Case 2).—Roentgenogram of the stomach interpreted as showing partial pyloric "obstruction" without evidence of marginal ulcer. At operation a large neoplasm was found obstructing the gastrojejunal stoma.

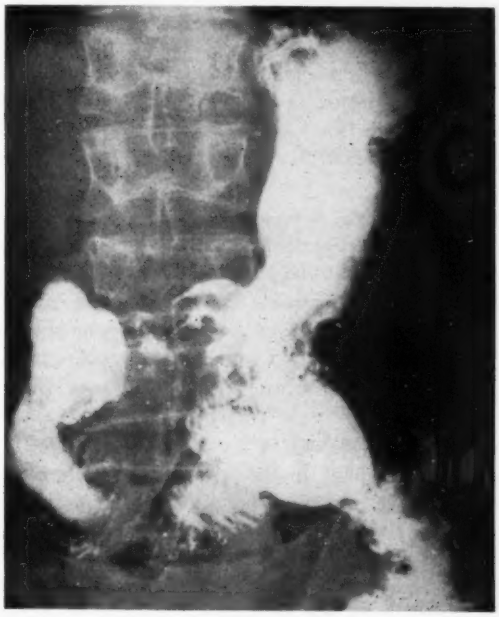

Fig. 3 (Case 3).—Roentgenogram of the stomach showing a deformed duodenal cap and a deformity of the antrum, interpreted as "gastric ulcer." A large neoplasm invading the prepyloric region of the stomach was found at operation.

(Fig. 2). The symptoms improved with conservative treatment, and the patient was discharged 21 days after admission, with a diagnosis of partial pyloric obstruction. He was readmitted nine months later with severe postprandial epigastric pain and persistent vomiting. Moderate tenderness was present, and a succession splash was elicited in the midepigastrium. The hemoglobin content was 15.4 gm. per 100 cc., and occult blood was present in the stools. The clinical diagnosis of marginal ulcer and complete pyloric obstruction was made. A 10-day period of conservative therapy consisting of gastric suction and antispasmodics failed to relieve the obstruction, and laparotomy was performed.

At operation a firm mass was found at the site of retrocolic gastrojejunostomy, and infiltration into the left transverse colon and body of the pancreas had occurred. A high subtotal gastric resection was performed. The microscopic sections revealed adenocarcinoma of the stomach infiltrating into the gastroenteric stoma with metastases to the gastrohepatic lymph nodes.

CASE 3.—M. J. E., a 57-year-old white man, was admitted to the hospital in November, 1952. He complained of constant epigastric pain, progressive weakness, a 21 lb. (19.5 kg.) loss of weight, and the passage of tarry stools. These symptoms had persisted for six months, and the patient had failed to improve on a medical regimen of antacids, antispasmodics, and bland diet.

There was a past history of a perforated duodenal ulcer in 1928, and in 1929 a gastroenterostomy had been performed. The patient remained asymptomatic until the onset of the present illness.

The physical examination on admission in November, 1952, was not remarkable except for tenderness in the midepigastrium and evidence of severe loss of weight. The hemoglobin content was 12.4 gm. per 100 cc., and occult blood was present in the stools. Histamine gastric analysis revealed achlorhydria. Roentgenographic examination of the stomach revealed a persistent deformity of the duodenal cap and a deformity in the antrum which suggested "ulcer" (Fig. 3). A clinical diagnosis of gastric ulcer was made.

At operation a large ulcerated neoplasm which involved the posterior wall of the prepyloric region of the stomach was found. The gastroenteric stoma was not involved by tumor. Microscopic sections revealed adenocarcinoma of the stomach.

## COMMENT

The possibility that gastric carcinoma may have been present at the time that gastroenterostomy was performed in the three cases in this series seems to be precluded by the passage of from 21 to 28 years between the time of gastrojejunostomy and the appearance of symptoms which seemed attributable to the gastric neoplasm.

The benign character of the symptoms, which are often associated with the development of gastric cancer in patients who possess a gastroenterostomy, is well illustrated in two of the patients in this series (Cases 1 and 2). These misleading symptoms and the difficulty in diagnosis are probably due largely to the location of the lesions in the antrum. Past history and early symptoms seemed to indicate a diagnosis of peptic ulcer in these two patients, and conservative therapy brought about temporary relief. The presence of a malignant neoplasm was suggested in the third patient (Case 3), however, by persistent epigastric pain, a 20 lb. (9.1 kg.) loss of weight, and progressive weakness.

The roentgenographic findings in this group of patients confirmed the observations of others that an accurate interpretation of lesions in the stomach distal to a gastroenteric stoma is extremely difficult.[3] In two of these patients antral defects were interpreted as representing "gastric ulcer" (Cases 1 and 2). In the third patient (Case 3) gastric retention was noted, although evidence of gastric deformity was not observed. Thus, in all three patients, roentgenographic examination of the stomach failed to demonstrate definite evidence of gastric neoplasm.

The finding in one patient (Case 1) of gastric acid values comparable to those obtained at the time of gastrojejunostomy illustrates the unreliability of gastric analysis in such cases.

Periods of conservative management which ranged from 9 to 12 months were instituted for two of the patients in the group under discussion. Additional investigation and surgical intervention were precipitated by the failure of the patients to gain significant relief from ulcer management. Other investigators have also reported that such patients received an initial course of conservative treatment before operation was undertaken.[5] From the results obtained both in the present series and in previous cases, it would appear that a patient in whom a gastric lesion develops after gastroenterostomy should be promptly subjected to operation. The customary diagnostic procedures are unsatisfactory in differentiating between a benign and a malignant lesion, especially when lesions are located in the portion of the stomach distal to the gastroenteric stoma. The institution of conservative measures in such cases might allow progression of the carcinoma to a stage where surgical intervention would be futile.

## SUMMARY AND CONCLUSIONS

Three cases in which gastric cancer developed 21 to 28 years after gastrojejunostomy for duodenal ulcer are reported. The literature is briefly reviewed. The difficulties encountered in diagnosis are discussed. From the evidence obtained from other reports and from the experience in these three cases, it appears that operative intervention should be undertaken promptly in patients in whom gastric lesions develop after gastrojejunostomy for duodenal ulcer.

5. Fischer, Clagett, and McDonald.[2] Gray and Lofgren.[3]

# ACUTE INTUSSUSCEPTION

## Analysis of One Hundred Sixteen Cases at St. Louis Children's Hospital

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AND
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ST. LOUIS

MANY ASPECTS of acute intussusception remain obscure or controversial. In the hope of contributing to etiology, diagnosis, treatment, and mortality factors, 116 consecutive cases at the St. Louis Children's Hospital from 1934 to 1951, inclusive, have been reviewed and analyzed.

TABLE 1.—*Incidence of Intussusception at Various Ages*

| Age, Months | Cases, No. |
|---|---|
| 1- 6 | 53 |
| 6-12 | 39 |
| 12-18 | 6 |
| 18-24 | 3 |
| Over 24 | 15 |

### INCIDENCE

*Frequency.*—During the 18-year interval there were 61,295 hospital admissions, giving a ratio of 1 : 528 for acute intussusception.

*Age and Sex.*—These were predisposing factors. Table 1 lists the number of cases of intussusception at various ages, ranging from 6 weeks to 9 years. More than one-half of all the cases, 53.4%, occurred from the fourth to the seventh month of age. Seventy-eight and four-tenths per cent of the patients were less than one year of age, and in 87% the condition had occurred by the age of 2 years. Sixty per cent were males. These figures for age and sex correspond closely to those published in other series.

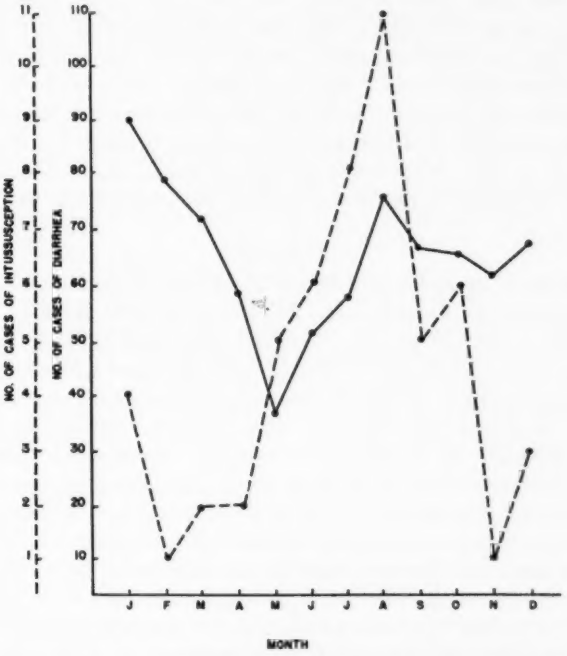
*Race.*—Of the 116 patients, 107 were white and 9 were Negro. This is the average proportion of white to Negro patients admitted to this hospital, and therefore does not suggest a difference in racial predisposition.

Assistance was given by Miss Shelley Ball and Mrs. Mildred Bernard, Record Librarians.

From the Department of Pediatrics, Washington University School of Medicine, and the St. Louis Children's Hospital.

*Heredity.*—A hereditary factor was suggested in only one instance, in which there was a history of occurrence of intussusception in a sibling. It is interesting to note that Close [1] cited five examples of familial intussusception in 146 reports from his total series of 363 cases.

*Seasonal Variation.*—Various authors have attached significance to the seasonal incidence of acute intussusception. Perrin and Lindsay [2] and Close,[1] reporting from London, England, noted their highest incidence in spring. Oberhelman and Condon,[3] of Chicago, found a minimal increase in late spring and late summer. In this regard Close made reference to Brown's [4] work concerning the seasonal variation of body




Seasonal incidence of nonspecific diarrhea and acute intussusception, 1945 to 1951.

lymphoid tissue, with a maximum in the summer months. If one accepts the attractive etiological theory of Perrin and Lindsay,[2] Brown's [4] observations are of relevant interest. The quantity of lymphoid tissue about the ileocecal valve and terminal ileum

1. Close, H. G.: Acute Intussusception in Children: A Statistical Analysis of 363 Cases at Guy's Hospital, Guy's Hosp. Rep. **81**:436, 1931.

2. Perrin, W. S., and Lindsay, E. C.: Intussusception: Monograph Based on 400 Cases, Brit. J. Surg. **9**:46, 1921.

3. Oberhelman, H. A., and Condon, J. B.: Symposium on Clinical Advances in Surgery: Acute Intussusception in Infants and Children; Analysis of 95 Cases in Cook County Children's Hospital, S. Clin. North America **27**:3, 1947.

4. Brown, W. H.: Constitutional Variation and Susceptibility to Disease, Arch. Int. Med. **44**:625, 1929.

is greatest in infancy, with progressive regression by the second year of life. Perrin and Lindsay hypothesized that inflammatory swelling of this tissue would explain both the peculiarity of age and the common site of origin of the intussusception in the terminal ileum or ileocecal valve. In our series there is a striking rise in the number of cases from May to September. This observation suggested a possible relationship to seasonal diarrhea. Perrin and Lindsay [2] could prove no such correlation in their series.

There were 777 patients with nonspecific diarrhea admitted to the St. Louis Children's Hospital in the seven-year period from 1945 to 1951. The seasonal incidence of the disease in these patients was determined and compared with that in 54 patients with acute intussusception admitted in this same interval. The Chart reveals a very striking similarity. The curves are roughly parallel, with the peak incidence of intussusception in August corresponding to one of the two maxima for diarrhea. This seasonal curve for diarrhea is similar to that originally published by Marriott, Hartmann, and Senn [5] in 1933. Their series included 318 patients seen in this hospital from 1930-1932, inclusive, and showed a rising incidence from June to September. Despite this seeming association, only 2 of the 116 patients had a history of diarrhea immediately preceding the acute onset of intussusception.

## ETIOLOGY

The etiology of acute intussusception in infancy is most often indeterminate. No evident cause could be found in 94.6% of the 610 cases reported by Gross and Ware,[6] in 83% of the 123 cases by Hogg and Donovan,[7] in 82.1% of the 95 cases by Oberhelman and Condon,[3] and in 96.4% of the 55 cases by Mayo and Woodruff.[8]

Demonstrable primary or contributory organic causes were seen more frequently in our series than is usually reported. Because of the difficulty in distinguishing cause from effect and the undetermined etiological significance of certain findings, it was not possible to arrive at an exact incidence. Meckel's diverticulum was present in 11 cases and acted as the apex of the intussusception in 9 of these. In the other two cases the diverticulum was just proximal to the invaginated bowel and may or may not have played a role in the initiation of the intussusception. In two cases it was initiated by adenomata of the ileum, and in another by a duplication cyst of the ileum. There were three instances of malposition of the cecum and associated abnormalities of mesenteric attachment due to malrotation. In two of these cases the excessive mobility of the bowel was believed to be responsible for the intussusception. In the third, a case of intussusception initiated by Meckel's diverticulum, death was indirectly attributable to the malrotation through the formation of an undetected postoperative volvulus of the ileum. In two patients the cecum was properly situated but was excessively mobile because of a long unattached mesentery. In six other cases particular mention was made of an unduly long mesentery of the small bowel.

5. Marriott, W. M.; Hartmann, A. F., and Senn, M. J. E.: Observations on Nature and Treatment of Diarrhea and Associated Systemic Disturbances, J. Pediat. **3**:181, 1933.

6. Gross, R. E., and Ware, P. F.: Intussusception in Childhood: Experiences from 610 Cases, New England J. Med. **239**:645, 1948.

7. Hogg, B. M., and Donovan, E. J.: Acute Intussusception in Infants and Children, Ann. Surg. **124**:262, 1946.

8. Mayo, C. W., and Woodruff, R.: Acute Intussusception, Arch. Surg. **43**:583, 1941.

In three cases intussusception was felt to be due to an extremely large ileocecal valve, which in two instances permitted intussusceptions of seven days' and three weeks' duration, respectively, without strangulation or serious injury to the bowel. Of uncertain significance was the presence of fibrous adhesive bands, varying in density from filmy strands to thick cords, in 13 cases. All were invariably present in the ileocecal-appendiceal region. Oberhelman and Condon [3] reported mesenteric glands to be of etiological significance in three cases. Marked mesenteric adenitis was noted in 14 of our cases. Reflecting on the acute onset of symptoms, generally in a well baby, we are regarding these as result and not cause of the intussusception, though the reverse may occasionally be true.

TABLE 2.—*Frequency of Symptoms and Signs*

| Symptoms and Signs | Cases | |
|---|---|---|
| | No. | % |
| Pain | 111 | 95.6 |
| Vomiting | 106 | 91.3 |
| Blood by rectum (by stool, rectal examination, or enema) | 93 | 80.1 |
| Abdominal and/or rectal (within) mass | 84 | 72.4 |
| "Shock" | 73 | 62.9 |

TABLE 3.—*Duration of Symptoms*

| Time, Hr. | Cases | |
|---|---|---|
| | No. | % |
| 12 | 39 | 33.6 |
| 24 | 27 | 23.2 |
| 48 | 23 | 19.8 |
| 72 | 13 | 11.2 |
| 96 | 6 | 5.17 |
| 96+ | 8 | 6.8 |

## SYMPTOMS AND SIGNS

The classical triad of sudden onset of abdominal pain, vomiting, and blood by rectum in infancy should be regarded as intussusception until proved otherwise. When such symptoms are also coupled with an abdominal mass, the diagnosis is fairly certain. Unfortunately, as seen from Table 2, the clinical picture is not always so complete.

Oberhelman and Condon [3] felt that "shock or impending shock as an early symptom is not adequately stressed in the literature." This impression, while undoubtedly shared by many observers, was first properly emphasized in the literature in 1940 by Gordon,[9] who wrote as follows: "In at least 4 patients who formerly had been very difficult to treat, it had seemed that they were eager and anxious to be examined. This may have been due to a state of shock for they all had a characteristic apathetic facial expression." We agree wholeheartedly with these authors. Though not the most constant, this finding was certainly the most striking in the clinical picture of our cases. The expression "shock" has been used rather loosely

9. Gordon, E. F.: Intussusception: Review of 42 Cases from Files of New Haven Hospital and 2 Cases Seen in Private Practice, Arch. Pediat. **57**:585, 1940.

to cover a wide variety of descriptive terms found in the history, depicting the general appearance of the patient. Terms such as "limp, drowsy, listless, lethargic, depressed, obtunded, stuporous, and unresponsive," were used to describe the patient on admission to the hospital in 73 cases. We consider this "knocked-out" appearance highly characteristic of the early stages of acute intussusception.

If an abdominal mass cannot be felt with certainty, one hesitates to make a diagnosis of acute intussusception. If the lethargy commented upon above is not present, it is not always easy to palpate the abdomen satisfactorily because of crying, restlessness, muscle guard, or abdominal distention. Furthermore, in several of our cases no abdominal mass was palpable even under preoperative anesthesia with good muscle relaxation. This is particularly true when the mass is in the region of the hepatic flexure beneath the liver edge and costal margin. In the absence of a palpable mass or of blood by rectum, though no definitive diagnosis can be made, it is the responsibility of the physician to realize the serious and surgical nature of the illness, and this perhaps constitutes the art of medical diagnosis.

### DURATION OF SYMPTOMS

In the whole group of 116 cases since 1934, the diagnosis of intussusception was made in 33.6% within 12 hours of onset. In 56.8% the duration of symptoms was less than 24 hours. These figures are praiseworthy and commend the diagnostic acumen of our local and rural physicians. Thinking that perhaps the awareness of the diagnosis of acute intussusception had increased in recent years, we compared the last 51 consecutive cases (August, 1945, to December, 1951) with the first 51 cases (February, 1916, to October, 1933) with reference to duration of symptoms. To our surprise, there was no significant difference in the two groups. The percentage of cases in which the diagnosis was made within 48 hours was identical in both groups (66.6%). There were 16 deaths in the earliest 51 cases, a mortality of 31.3%, compared with 3 deaths, a mortality of 5.8%, in the last 51 cases in this hospital. Since this sharp decline is obviously not due to earlier diagnosis, it points to improvements in preoperative, surgical, and postoperative care. Hogg and Donovan,[7] comparing a series of 123 cases from 1927 to 1945 with a previous series from the same hospital reported by Bolling [10] in 1923, also found that the drop in mortality, from 30% to 13%, was in no way related to any appreciable decrease in duration of illness. Ladd and Gross,[11] however, felt that time was an important factor and noted a 38% mortality in their original series in those cases with duration of symptoms of 96 hours or more.

Fourteen of our 116 patients had signs and symptoms of intestinal obstruction for 96 hours or longer. Eight of these had irreducible or gangrenous small and/or large bowel. Four of the 14 patients died, a mortality of 28.5%. Of particular interest to us were the other six patients in this group in whom the bowel was viable despite signs and symptoms of progressive intestinal obstruction and strangulation. The ages of these patients were 4 months, 6 months, 9 months, 19 months, 3½ years, and 5 years—a generous proportion of older infants and children. Four of these

10. Bolling, R. W.: Acute Intussusception in Infants, Ann. Surg. **78**:349, 1923.

11. Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infancy and Childhood, Philadelphia, W. B. Saunders Company, 1941.

patients had symptoms of more than 96 hours' duration—5, 6, 7, and 21 days, respectively. Even though the history in the last case suggested acute intussusception because of the long duration of the symptoms, that diagnosis was discarded in favor of a retroperitoneal cyst or tumor. At operation, intussusception was found extending to the splenic flexure. The terminal ileum had intussuscepted through a very large ileocecal valve. The latter finding was present in another case in this same group and was believed to play an important part in maintenance of bowel viability.

### TEMPERATURE

The rectal temperature on admission was over 37 C. (98.6 F.) in 91.3% of our cases but over 38 C. (100.4 F.) in only 45.6%. There were 23 patients with admission temperatures of 39 C. (102.2 F.) or more. These were studied in relation to duration of symptoms, presence of gangrenous or irreducible bowel, and fatality. Temperature elevation bore no direct relation to duration of symptoms. Sixteen of these 23 patients had symptoms of 48 hours' duration or less. In contrast, there was an apparent correlation of temperature elevation with morbidity and mortality.

TABLE 4.—*White Blood Cell Count and Duration of Symptoms*

| | | Duration of Symptoms | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 12 Hours | | 24 Hours | | 48 Hours | | 72 Hours | | 96 Hours and Longer | |
| White Cells, No. | Cases, Total No. | No. Cases | % | No. Cases | % | No. Cases | % | No. Cases | % | No. Cases | % |
| Under 10,000 | 40 | 8 | 20.0 | 8 | 20.0 | 9 | 22.5 | 9 | 22.5 | 6 | 15.0 |
| 11,000-20,000 | 60 | 28 | 46.6 | 11 | 18.3 | 11 | 18.3 | 5 | 8.3 | 5 | 8.3 |
| 21,000-30,000 | 11 | 2 | 18.1 | 7 | 63.6 | 2 | 18.1 | .. | .... | .. | .... |
| 31,000-40,000 | 3 | 1 | 33.3 | .. | .... | 2 | 66.6 | .. | .... | .. | .... |

One-half of the fatal cases and 29.4% of the cases with gangrenous or irreducible bowel fell in this group.

### BLOOD PICTURE

Scant attention has been paid to the blood picture in acute intussusception. Gordon,[9] reviewing the literature to 1940, concluded that the white blood cell count and differential were of no value. He also considered that the white blood cell counts in his 44 cases were not helpful. These counts varied from 6,250 to 52,000, with polymorphonuclear predominance in 32% to 94%. Gibbs and Sutton [12] reported admission leucocyte counts in 55 of their 92 cases. In 39 cases, or 70.9%, these were over 10,000. Differential counts were not reported. Oberhelman and Condon [3] refer to the blood picture as "within relatively normal limits" except in those patients who had been ill for several days. In their latest review of 610 cases of intussusception in childhood, Gross and Ware [6] made no reference to the blood findings. An analysis of the white blood cell and differential count in our patients appears to be of both diagnostic and prognostic value. There were 114 recorded admission white cell counts. These ranged from 3,600 to 40,300. Sixty-four and nine-tenths per cent were over 10,000.

12. Gibbs, E. W., and Sutton, P. W.: Intussusception: 92 Cases in Infancy and Childhood, Surgery **14**:708, 1943.

It is apparent from Table 4 that no correlation can be made between elevation of the white blood cell count and duration of illness. In the group of cases with counts under 10,000, the percentage of cases was for all purposes the same, irrespective of duration. Furthermore, in the group of cases with definitely elevated white cell counts (more than 20,000 in 14 cases) the illness in all was of less than 48 hours' duration. There were 106 recorded differential counts with immature forms (stab forms, juvenile forms, and myelocytes) ranging from 1 to 74%. By contrast with the total white blood cell count, there was a striking increase in immature leucocytes with increasing symptom duration.

Table 5 reveals that in 69.7% of the cases with less than 20% of young forms the symptoms were of 24 hours' duration or less, whereas in the group of cases with more than 20% young forms, 70% were of more than 24 hours' duration.

Of particular interest was the apparent direct relationship of the left shift in the Schilling differential to gangrenous and irreducible bowel and to death. The incidence of nonviable bowel increased from 7.8% with 20% or less of young forms to

TABLE 5.—*Percentage of Immature Leucocytes and Duration of Symptoms*

| Duration of Symptoms, Hr. | No. Cases | |
|---|---|---|
| | Less than 20% Immature Leucocytes | More than 20% Immature Leucocytes |
| 12 | 33 | 4 |
| 24 | 20 | 5 |
| 48 | 10 | 9 |
| 72 | 7 | 7 |
| 96 and longer | 6 | 5 |
| Total | 76 | 30 |

53.8% with 31% or more immature cells. Likewise, the mortality increased from 1.3% in the cases with less than 20% young forms to 38.4% in the cases with 31% or more immature leucocytes.

### SIGNIFICANCE OF PROGRESSION OF THE INTUSSUSCEPTION

The distance to which the intussusception had traveled was evaluated with reference to duration of symptoms and prognosis. There were 17 cases of intussusception to the level of the rectosigmoid. In 16 of these the apex of the invaginated bowel was palpated in the rectum. In 13 of these cases, or 76.4%, the symptoms were of 48 hours' duration or less. This lack of correlation between symptom duration and advancement of the intussusception has been confirmed by Perrin and Lindsay [2] and by Oberhelman and Condon.[3] Likewise, in agreement with these authors, we could not relate mortality with progression of the intussusceptum. This is at variance with Ladd and Gross,[11] who found a progressive rise in mortality the more caudal the intussusceptum. Their mortality for intussusceptions which had progressed to the rectum was about 50%. In 12 of our 17 cases with far advanced intussusception, the invaginated bowel was manually reduced and found to be viable. The bowel was gangrenous in four cases and irreducible in the fifth. Three of the latter group were fatal, a mortality of 17.6% in this total group of rectosigmoid intussuscepta.

### SPONTANEOUSLY REDUCED AND/OR RECURRENT INTUSSUSCEPTION

There were eight patients not included in this review in whom a clinical diagnosis of acute intussusception was made and who did not come to surgery because of apparent spontaneous reduction or inadvertent reduction by barium enema in the visualization of the colon for diagnostic purposes. In another seven patients with classical history and corroborative clinical and/or x-ray evidence, no intussusception was found at surgical exploration. All showed evidence of recent spontaneous reduction. Tell-tale signs were serous peritoneal fluid, mesenteric adenitis associated with edema and inflammation of ileum and colon, and subserosal intestinal hemorrhages. Another five patients showed almost complete reduction of the intussusception at laparotomy. Preoperatively, these had shown clinical evidence of further advanced intussusception, and in two involvement of more distal bowel was visualized by barium enema.

There were three patients in whom the intussusception had apparently become reduced spontaneously on one or more occasions, only to recur and necessitate surgery. One 5-month-old infant had been admitted previously with symptoms of acute intussusception of three days' duration. A mass was palpated in the right lower quadrant of the abdomen, and blood and mucus were present on the rectal examining finger. When the patient was seen by the surgeons one hour later, the mass was no longer palpable. It was decided to observe the patient closely. During the first two days of hospitalization, the stools contained blood and mucus. There was some degree of vomiting for four days. Prior to discharge, on the sixth day, the infant appeared perfectly well; there was no vomiting, no abdominal mass, and the stools were normal. The patient was readmitted three days later with a history of colic and vomiting since discharge. On exploration, an irreducible and gangrenous intussusception, involving terminal ileum and cecum, was found. This was considered to be a recurrent lesion. From the history and clinical appearance of the child it seemed unlikely that the intussusception had persisted from the onset of illness 12 days previously.

Another infant had a past history of four episodes of mucoid diarrhea, vomiting, and colicky pain. On one of these occasions, six months previously, in addition to these symptoms there was passage of bright blood by rectum. When seen later in the day, the infant appeared well; there were no abnormal physical signs, and it was presumed that an intussusception had been reduced spontaneously At the age of 10 months the patient was readmitted with complaints of crampy abdominal pain, vomiting, and diarrhea for three days. No abdominal mass was palpable, but blood was passed by rectum. In view of the past history, it was felt that exploratory laparotomy was indicated. At operation a viable intussusception of the ileum to the level of the hepatic flexure was found.

A third infant, 3 months old, had had an onset of pain, vomiting, and passage of blood and mucus by rectum 16 hours prior to admission. No abdominal mass was palpable. Barium enema outlined the colon to the splenic flexure only. At laparotomy an intussusception of the transverse colon into the descending colon was found and easily reduced. Because of the presence of barium in the lumen of the cecum at exploration, it was concluded that the original intussusception visualized by barium had been reduced spontaneously, allowing barium to enter the proximal large bowel, and then had re-formed. Death occurred 48 hours postoperatively in this case.

Autopsy revealed a newly formed recurrent intussusception of the terminal ileum into the colon to the level of the splenic flexure. Just beyond the obstruction and corresponding to the site of the original intussusception reduced at the time of surgery, there was hyperemia of the intestinal wall.

There was one case in which two laparotomies were performed for intussusception. At the age of 7 months an ileocolic intussusception to the rectosigmoid region was manually reduced and viable. Two years later there was a recurrence of intussusception to the level of the midtransverse colon.

### TREATMENT

In no case was nonsurgical reduction of the intussusception purposefully attempted. There were, however, eight patients with signs and/or symptoms of intussusception who did not require surgery, and another seven patients who showed evidence of recent spontaneous reduction at the time of exploration. These have been discussed under the section on recurrent and spontaneously reduced intussusception. Table 6 lists the various operative procedures performed in the 109 intussusceptions

TABLE 6.—*Operative Procedures in 109 Intussusceptions*

| Operative Procedure | No. Cases | No. Deaths |
|---|---|---|
| Manual reduction | 90 | 2 |
| Manual reduction + removal of Meckel's diverticulum | 2 | .. |
| Resection and anastomosis without enterostomy | 7 | 4 |
| Resection and anastomosis with enterostomy | 5 | 1 |
| Exteriorization | 3 | 1 |
| Enterostomy (gangrene—no resection) | 1 | 1 |
| Enterocolostomy (gangrene—no resection) | 1 | 1 |

found present at laparotomy. Ninety, 82.5%, were reduced manually by taxis. In 17 cases, 15.5%, there was gangrenous or irreducible bowel. These are discussed subsequently.

*Additional Operative Procedures.*—Considerable controversy exists concerning removal of the appendix in these patients. Proponents of appendectomy, Peterson [13] and Goldman and Elman,[14] have either claimed that appendiceal inflammation played a role in initiating intussusception or that the procedure was indicated for prevention of recurrence by virtue of the formation of adhesions. Others are strongly antagonistic to any additional surgical procedure. Their chief objections are that (1) opening the intestinal tract permits soiling of the peritoneum in the face of bowel with various degrees of circulatory impairment; (2) the extra time required is an added and unnecessary liability to the acutely ill patient, and (3) the inverted stump has occasionally been the site of a recurrent intussusception.

There were 51 appendectomies in our series. In 39, the stump was inverted; in 7 it was not, and in another 5 no reference was made to this point. Since there were no fatalities in this group of patients, appendectomy done when the condition of the patient permits does not appear to be an added risk. One of the most serious

13. Peterson, E. W.: Acute Intussusception in an Infant: Resection of Gangrenous Intussusceptum; Murphy Button Anastomosis; Recovery, M. Rec. **67**:334, 1905.

14. Goldman, L., and Elman, R.: Spontaneous Reduction of Acute Intussusception in Children: Its Incidence and Significance in Diagnosis and Treatment of Recurrent Intussusception, Am. J. Surg. **49**:259, 1940.

objections to any additive surgical procedure, the threat of peritonitis, is undoubtedly minimized today by the use of chemotherapy and/or antibiotics.

To prevent recurrence of the intussusception, bowel fixation by plication of mesocolon or suturing the terminal ileum to the ascending colon was performed in 12 cases. In eight instances, these procedures seemed warranted because of redundant mesocolon, undescended cecum, or a very large ileocecal valve. The relative merits or drawbacks to these additional surgical measures were considered in respect to the seven cases of intestinal obstruction due to adhesive bands occurring from two months to three and one-half years postoperatively. Four of the seven patients, 57.1%, were seen within three months. Three of these seven patients with postoperative intestinal obstruction had had appendectomy in addition to manual reduction of the intussusception. In one of these, the appendix was gangrenous, and removal was mandatory. In this case, the ileum was also sutured to the ascending colon. In three of the four remaining patients, bowel fixation had been attempted.

Since appendectomy was performed in 44% of our cases, this procedure cannot be incriminated with respect to postoperative adhesions. On the other hand, procedures such as cecopexy, colopexy, or mesenteric plication, which were performed in four out of seven, or 57.1%, of the cases of postoperative intestinal obstruction

TABLE 7.—*Duration of Symptoms in Cases with Gangrenous or Irreducible Bowel as Compared with Other Cases*

| Duration of Symptoms | 12 Hours | 24 Hours | 48 Hours | 72 Hours | 96 Hours and Longer |
|---|---|---|---|---|---|
| Total no. cases | 39 | 27 | 23 | 13 | 14 |
| No. cases gangrenous or irreducible bowel | .. | 2 | 3 | 4 | 8 |

due to adhesive bands, seem inadvisable. Nor can it be said that these measures are of definite value in preventing recurrence. Our sole patient with recurrent postoperative intussusception (excluding the case discovered at autopsy) had had the ileum sutured to the cecum as prophylaxis against recurrence.

### SEVENTEEN CASES WITH GANGRENOUS AND IRREDUCIBLE BOWEL

The incidence of gangrenous or irreducible small and/or large bowel (excluding gangrene of Meckel's diverticulum or appendix alone) was 14.6%—17 cases. None were of less than 12 hours' duration, and 70.5% were of more than 48 hours' duration (Table 7). In this group of 17 cases with gangrenous or irreducible bowel, there were eight deaths and nine survivals—a mortality of 47%. In an attempt to determine mortality factors, these two groups were compared from several aspects.

*Age, Duration of Symptoms, Progression of the Intussusceptum.*—Of possible significance was the greater proportion of older infants among the survivors. The duration of symptoms was essentially the same in the two groups. The two groups were also comparable with reference to the advancement of the intussusception.

*Operative Procedures.*—The fatal group was weighted by two cases of irreducible intussusception in which surgical measures consisted only of enterostomy in one case and enterocolostomy in the other without resection of the gangrenous intussusception.

*Meckel's Diverticulum.*—There were three instances of Meckel's diverticulum [15] in each of the two groups. In one of the nonfatal cases with gangrenous irreducible bowel, the diverticulum was just proximal to and apparently not involved in the intussusception at the time of exploration.

*Drug Therapy.*—With one exception, all the fatal cases complicated by gangrenous bowel occurred prior to 1946. Of the nine recoveries in the group with nonviable bowel, six occurred after 1946. The addition of streptomycin to penicillin and sulfonamides appears to have been a factor in reduction of mortality in the cases with gangrenous bowel. Relevant to the evaluation of drug therapy in these cases were the number of hours before operation that drug therapy was started and the time of death. Surgery was performed within 7.3 hours in the nonfatal group, and within 5.1 hours in the fatal group, and the two groups are thus comparable. Four of the deaths occurred within 10 hours postoperatively and another two within 48 hours. Two who died were patients who had survived for 27 and 30 days, respectively. One intussusception occurred in 1939, and the patient received sulfapyridine only. The intussusception had been left in situ with enterostomy. Two weeks postoperatively the intussusception sloughed off into the abdominal incision. Autopsy revealed, in addition, bronchopneumonia and pleurisy. The use of antibiotics in this case would undoubtedly have been helpful. In the other case (in 1945) exteriorization had been performed. Despite the use of sulfadiazine, sulfamerazine, and penicillin throughout the illness, the postoperative course was complicated by peritonitis, bronchopneumonia, otitis media, and urinary infection. The latter cases emphasize that chemotherapy and antibiotics are not a replacement for adequate surgery.

### OVER-ALL MORTALITY

There were 10 deaths in the entire series of 116 cases, a mortality of 8.6%. In seven of the fatal cases symptoms were of more than 48 hours' duration. Four of the fatal cases were complicated by a Meckel's diverticulum acting as the apex of the intussusception. Two deaths occurred in the group of manually reduced intussusceptions with viable bowel. In one case with intussusception of 16 hours' duration, death occurred 48 hours postoperatively. At autopsy an undetected recurrent intussusception was found. The other case was of 72 hours' duration and was initiated by a Meckel's diverticulum. Both bowel and diverticulum were viable and not resected. Death occurred five hours postoperatively. Autopsy revealed malrotation of the cecum with volvulus of the small bowel.

In the eight remaining fatal cases, there was extensive gangrene of large and/or small bowel. In two of these, the irreducible gangrenous intussusception was left in situ with enterostomy and enterocolostomy as temporizing procedures. In five cases, resection of gangrenous bowel with primary anastomosis was performed, and in another exteriorization was carried out. One of the fatalities in the latter group was due to acute hemolysis complicated by hemoglobinuria and convulsions, believed to be caused by the injudicious use of hyaluronidase, which allowed too rapid absorption of M/6 ammonium chloride given subcutaneously for the correction of hypochloremic alkalosis.

15. To be reviewed in a subsequent report.

SUMMARY

One hundred and sixteen cases of acute intussusception (1934 to 1951) have been analyzed from the following aspects:

1. Age, sex, race, heredity.

2. Seasonal variation. Though the graphs for seasonal incidence of diarrhea and acute intussusception were remarkably similar, in only 2 of the 116 cases was there a history of preceding diarrhea.

3. Etiology. Direct or contributory causes were found in a relatively large number of patients.

4. Symptoms and signs. Diagnostic significance has been attached to the "knocked-out" appearance seen so commonly even in the early stages of acute intussusception.

5. Duration of symptoms. In 33.6% the diagnosis was made correctly within 12 hours of onset of symptoms; in 56.8% within 24 hours of onset. Sharp decline in mortality rates in the last two or three decades appears to be due to improved preoperative, surgical, and postoperative care rather than earlier diagnosis.

6. Temperature. Elevations of 39 C. (102.2 F.) or higher were of prognostic significance. One-half of the fatal cases and 29.4% of the cases with gangrenous or irreducible bowel fell in this group.

7. Blood picture. Elevation of the white blood cell count bore no relation to symptom duration. On the other hand, there was a striking increase of the left shift in the Schilling differential count with increasing symptom duration, and the extent of this shift varied directly with the incidence of gangrenous and irreducible bowel and death.

8. Progression of the intussusception. Neither symptom duration nor mortality could be correlated with progressive advancement of the intussusception.

9. Spontaneously reduced and recurrent intussusception.

10. Treatment. An analysis of surgical notes permitted an evaluation of additional procedures such as appendectomy and bowel fixation. Appendectomy was performed in 44% of the cases. Since there were no fatalities in this group, the procedure did not appear to be an added risk, provided that the condition of the patient was not critical. Bowel fixation was performed in 12 cases as prophylaxis against recurrence. In four of these cases the procedure was followed by intestinal obstruction due to adhesive bands. Since this number constitutes 57.1% of all the cases of postoperative adhesive intestinal obstruction, procedures such as cecopexy, colopexy, or mesenteric plication seem highly inadvisable. Furthermore, the value of these measures in preventing recurrence remains unproved.

11. Cases with gangrenous and irreducible bowel. In the 17 cases with gangrenous and irreducible bowel, there were eight deaths and nine survivals. The fatal and nonfatal groups were compared with respect to age, duration of symptoms, progression of the intussusception, operative procedures, presence of Meckel's diverticulum, and use of chemotherapy and antibiotics.

12. Mortality. The 10 fatal cases (mortality of 8.6%) were briefly described.

# RADIOIODINE TRACER AND BIOPSY IN THE DIAGNOSIS AND TREATMENT OF HYPERTHYROIDISM

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CLASSIFICATION of diseases of the thyroid has been oversimplified. Excluding tumors and infections, there has been a trend to consider all thyroid conditions as being one of three varieties, namely, hypothyroid, euthyroid, and hyperthyroid. If it were accurate, this would constitute an ideal state of affairs from the standpoint of the clinician as well as the patient.

The radioactive iodine tracer test has been considered by many [1] to be the "final word" in this business of herding all thyroids into one of these appropriate stalls. Having had some small measure of experience [2] with radioiodine tracer studies, I began to notice this tendency toward an empirical attitude with regard to the diagnosis of thyroid disease. On the other hand, with the passage of time some overly severe [3] and possibly unscientific criticism of the procedure has arisen.

In this paper suggestions for the better use of this diagnostic tool are given, although its shortcomings are clearly recognized. Examples of some provocative types of situations encountered in dealing with possible cases of hyperthyroidism will be given. The further possibilities of exploration will at once be obvious, even as it becomes apparent that the former simple empirical methods of defining, diagnosing, and treating thyroid disease must undergo a revision.

The fact has emerged clearly from this study that there are three important tests which must be made in every questionable case of possible hyperthyroidism. There are (1) the radioiodine tracer test, (2) the basal metabolic rate determination, and (3) the microscopic study of representative sections of the thyroid gland. Although there are other tests of interest, such as protein-bound iodine, conversion ratios, thyroid secretory rates, cholesterol, and thyrotropin, it is not felt that these are necessary in obtaining a classification of the case that is reasonably correct from a clinical standpoint.

Protein-bound $I^{131}$, while a far better diagnostic criterion [4] than total plasma $I^{131}$, is too erratic to be reliable.[2] The chances for technical errors are numerous, a variation of over 100-fold being seen in euthyroid subjects.

1. Jaffe, H. L., and Ottoman, R. E.: Evaluation of Radioiodine Test for Thyroid Function, J. A. M. A. **143**:515, 1950.

2. Seed, L.; Jaffe, B., and Baumeister, C.: The Tracer Dose of Radioactive Iodine in the Diagnosis of Thyroid Disease, J. Clin. Endocrinol. **11**:1143, 1951.

3. McAdams, G. B., and Salter, W. T.: Comparative Tests of Thyroid Function, Ann. Int. Med. **36**:1198, 1952.

4. Chaikoff, I. L.; Taurog, A., and Reinhardt, W. O.: The Metabolic Significance of Protein-Bound Iodine of Plasma: A Study of Its Concentration Under Various Conditions and of Its Rate of Formation as Measured with Radioactive Iodine, Endocrinology **40**:47, 1947. Harsha, W. H.: Use of Protein Bound Iodine as Clinical Tool, J. Kansas M. Soc. **51**:332, 1950.

The ratio between the quantity of $I^{131}$ bound to protein (presumably the thyroxine fraction) and the total plasma $I^{131}$, is called the conversion ratio. It is felt by many to be the most accurate test from a statistical standpoint.[5] While a good deal of extra labor and some expense is required, it is certainly superior to the protein-bound $I^{131}$ test. When one looks at this test in retrospect, the annoying fact arises that it is based on a ratio between two factors, one of which (plasma $I^{131}$) is felt to be almost worthless and the second of which (protein-bound $I^{131}$) is subject to wide variation and many technical errors.

To be of any value, the laboratory work must be correlated with the clinical picture. The symptoms, about which each patient was carefully asked, were increased appetite, palpitation, nervousness, fatigability, sweating, and heat sensitivity. The signs checked in each case were the following: raised pulse pressure, fast pulse rate, loss of weight, eye signs, thyroid enlargement, moist flushed palms, and tremor. In making a final evaluation, the clinical picture after treatment was compared with the pretreatment status.

### DESCRIPTION OF TECHNIQUE USED IN RADIOIODINE TRACER TESTS [2]

*General.*—The 24-hour pickup of $I^{131}$ by the thyroid gland and the 24-hour urinary excretion were determined on all patients.

*Tracer Dose.*—A 50 $\mu$c dose of carrier-free $I^{131}$ is measured out and placed in a 25 ml. volumetric flask. Distilled water is added to increase the volume to exactly 25 ml. Each dose is assayed at three distances, chosen so that the second distance gives half the number of counts given by the first or shortest distance, and the third distance, one-third the number of counts. These distances as measured from the center of the flask (the center of radiation) to the center of sensitivity of the Geiger-Mueller counter tube are (*a*) 23.5 cm., (*b*) 33.5 cm., and (*c*) 41.0 cm. If the measurement is made from the front of the 25 ml. flask to the tube, it will simulate almost exactly the measurement from the skin to the tube. The center of radiation in a 25 ml. flask is approximately 2 cm. from the front of the flask, and the center of radiation of the thyroid gland is only a trifle over 2 cm. from the skin surface. Thus, if one assays a quantity of $I^{131}$ in a 25 ml. flask at a distance measured from the front of the flask to the tube, one should obtain practically the same number of counts as obtained for the same quantity of $I^{131}$ in the thyroid gland at a distance measured from the skin to the tube. The isthmus of the thyroid gland crosses the trachea just below the cricoid cartilage. The skin measurement is taken from a point on the center of the neck 1 cm. below the cricoid cartilage. All three measurements are used in the calculations. It would be probably more accurate to use only the counts from the two farthest distances.

The Geiger counter is calibrated and the number of counts per microcurie is known. The presumed 50 $\mu$c dose is corrected to 48 or 52 $\mu$c or to whatever the reading indicates. This correction is not necessary in the calculation of thyroid

5. Williams, R. H.; Jaffe, H., and Bernstein, B.: Comparisons of the Distribution of Radioactive Iodine in Serum and Urine in Different Levels of Thyroid Function, J. Clin. Invest. **28**:1222, 1949. Sheline, G. E., and Clark, D. E.: Index of Thyroid Function: Estimation by Rate of Organic Binding of $I^{131}$, J. Lab. & Clin. Med. **36**:450, 1950. Clark, D. E.; Moe, R. H., and Adams, E. E.: The Rate of Conversion of Administered Inorganic Radioactive Iodine into Protein-Bound Iodine of Plasma as an Aid in the Evaluation of Thyroid Function, Surgery **26**:331, 1949.

pick-up, which is entirely a percentile relationship of two sets of counts, but it is useful in calculating percentage of urinary output, which is a percentile relationship between the number of microcuries given, as determined by one counter, and the number excreted, as determined by another counter.

The dose is given in the morning, preferably with the patient fasting. It is not essential that the patient fast completely. We have found that an empty stomach and the nervousness accompanying the visit to the laboratory and the drinking of the "atomic cocktail" occasionally induce vomiting. Radioactive vomitus is definitely a nuisance. If the patient has a piece of toast and a cup of coffee, it does not interfere with the 24-hour determinations and it eliminates the vomiting episodes.

The patient must not be taking thyroid medication, antithyroid drugs, or iodine. If he is receiving antithyroid therapy with iodine or propylthiouracil, it is discontinued for one week. The dye used in an x-ray examination of the gall bladder interferes for about three weeks and in an x-ray examination of the desiccated thyroid, for about the same length of time.

*Geiger-Mueller Counter.*—In all these determinations a bismuth-wall gamma-ray counter measuring 1 by 8½ in. (2.5 by 21.5 cm.) was used. Its high efficiency for iodine gamma-ray counting makes it necessary to use an absorber to eliminate scattered radiation. The tube is enclosed in an ½ in. (1.2 cm.) lead shield with an opening in the side as long and as wide as the bismuth cathode screen. Over the opening is placed a sheet of lead, 1.2 gm. per square centimeter (0.045 in. thick), to act as an absorber. In a mock study, a hollow glass thyroid was blown up to simulate a normal thyroid gland. Twenty-five microcuries of $I^{131}$ was placed in it, and the glass thyroid was suspended in a 1,000 ml. beaker, with the front of the simulated gland 1 cm. from the inner wall of the beaker. Counts were taken without an absorber, both with the beaker empty and with the beaker full of water. When the beaker was filled with water, there was almost a 25% increase in counts due to scatter. These secondary waves are much weaker than the $I^{131}$ gamma waves and can be removed by absorption. If a sheet of lead, 1.2 gm. per square centimeter is placed in front of the tube, the counts are identical both when the beaker is empty and when it is full of water. In short, the absorber eliminates the spurious counts without too much reduction (30%) in the total number of counts. This experiment was repeated by removing the thyroid gland from a fresh cadaver and replacing it with the glass model filled with a solution of $I^{131}$. The results were the same. In counters of low efficiency the scattered rays and spurious counts are not too important, but with tubes of high efficiency the error is quite large.

The tube is used in a longitudinal direction over the neck. The findings are practically the same whether the tube is placed transversely or longitudinally, but, since the variation of the position of the thyroid gland is more in an up-and-down, rather than a transverse, direction, a rectangular-shaped portal gives better results if placed parallel with the longitudinal axis of the neck.

*Calculation of Thyroid Pick-Up.*—Counts are made over the neck at three distances as measured from the skin to the center of the tube: (*a*) 21.5 cm., (*b*) 31.5 cm., and (*c*) 40.0 cm. With a 10% pick-up (5$\mu$c) the net counts are approximately (*a*) 600, (*b*) 300, and (*c*) 200 per minute. All of the counts are registered for two minutes. When the pick-up is low, the time is increased to give a minimum of 500 net counts at the farthest distance.

A count is taken with the tube against the thigh. This reading is deducted from the thyroid readings, as representing background and soft tissue radiation. In a large series of readings the counts from the second distance have averaged exactly half of those from the first distance, and from the third distance they have averaged a third of those from the first distance. There have been, of course, sharp variations. If the second and third counts are higher than the respective 50 and 33%, the thyroid gland is more deeply placed than estimated; if the second and third counts are less than 50 and 33%, the gland is closer to the skin than was estimated.

A correction can be made for this error by mathematical calculation or by actually measuring the percentage shifts in the second and third counts when a center of radiation is shifted 1 to 3 cm. Most of the determinations were not corrected in this manner. The sum of the corrected readings is divided by 0.91 to correct for decay and then compared with the counts made on the sample on the previous day.

*Calculation of Urinary Output of* $I^{131}$.—Two hundred milliliters of urine is placed in a Marinelli beaker and counted through a calibrated cylindrical tube. The number of microcuries excreted is calculated, corrected for decay, and compared with the number of microcuries administered, as determined by the preliminary assay with the bismuth-cathode counter.

## REPORT OF CASES

CASE 1.—Mr. T. S., a 37-year-old salesman, was seen in consultation on Oct. 2, 1950. He had been feeling very nervous for two or three years and was losing energy. If he went out for a social evening, he would become nauseated and perspire a great deal. To control this tension he would take fair amounts of liquor. His temper had tended to become very bad. There was mild shortness of breath and a feeling of compression around the neck and some palpation.

On examination there was thought to be moderate enlargement of the right lobe of the thyroid. The blood pressure was slightly labile, ranging from 122/80 to 140/80, the pulse rate being normal at 80. The weight was unchanged at 162 lb. (73.5 kg.), this being about normal for his 69 in. (175.2 cm.) in height. The eyes were not prominent. The palms were moist, but not warm. There was a 3+ fine tremor of the hands.

The basal metabolic rate was essentially normal, being —1%. The radioiodine tracer test was strongly positive (pick-up of 85.5% and urinary excretion of 20.86% with total 106.36%). The patient was operated on Oct. 30, 1950, after being given strong iodine solution U. S. P. for two weeks. Most of the thyroid was removed on the left, and a small piece of the thyroid (1 cc.) was allowed to remain on the right, a total of 6.1 gm. being resected. Histological section showed a normal thyroid gland.

For six months after surgery the patient was much less nervous, the tremor disappeared, and he was not nauseated. No signs of hypothyroidism developed. Trace was lost of him after this time.

*Comment.*—This patient obviously had a neurosis, but the symptoms of the neurosis rather closely mimicked those of hyperthyroidism. It is true that the only positive signs in this patient were those which can be found with anxiety neurosis. However, the positive radioiodine tracer test swung the decision in favor of surgery.

An interesting sequel to this mistaken surgery was the patient's sense of well-being. This cannot be attributed to hypothyroidism, since no symptoms and signs of this condition developed. It quite possibly was due to the well-known beneficial effects of surgery of a supposedly curative nature in cases of anxiety neurosis (i. e.,

concentration of the patient's troubles into one organ and then removing the hostile organ). This is more frequently seen in the temporary cure of a spastic colon by the mistaken removal of a supposedly diseased, but actually normal, appendix.

These neurotic patients often have a falsely elevated basal metabolic rate (although this patient had a normal basal metabolic rate owing to extreme care in conducting the tests). This elevated basal metabolic rate coupled with a falsely positive radioiodine tracer test would certainly tend to indicate surgery. Just why some of these patients have a falsely positive tracer study is not apparent, but the fact remains that a number of them do.

In the case illustrated the symptoms of hyperthyroidism were mimicked by a single condition, i. e., anxiety neurosis. In other patients, who did not have anxiety neurosis but who did have falsely positive tracer studies and histologically normal thyroid glands, the symptoms were mimicked by several coexisting conditions. For example, one patient had (1) coronary heart disease, (2) postsurgical menopausal syndrome, and (3) biliary dyskinesia and multiple diverticula of the colon.

This case illustrates the fact that cases of supposed hyperthyroidism should be rather classic as regards the clinical picture (symptoms and signs) and the laboratory studies (basal metabolic rate and radioiodine tracer studies). Otherwise, thyroid biopsy should be done before one contemplates any definitive surgical or medical therapy.

CASE 2.—Mrs. J. T., a 48-year-old housewife, was first seen on June 9, 1950. For the last year the patient had been bothered with moderate dyspnea and attacks of palpitation. She had noticed mild nervousness and fatigability and some increase in sweating. For about two years she had increasing numbers of attacks of tingling and numbness in the right extremities, accompanied by strange odors, dizziness, and faintness.

On physical examination the thyroid was firm and rather enlarged. There had been a weight loss of 10 lb. (4.5 kg.) in the past year.

The basal metabolic rate was + 5%. The radioiodine tracer test was thought to be positive because the sum of the pick-up (49%) and the urinary excretion (51%) equaled 100%. Preoperative iodine therapy was used for two weeks. On July 14, 1950, approximately 53.5 gm. of thyroid was removed, about one-third of the gland being allowed to remain in situ. Histological study showed a diffuse parenchymatous goiter with marked involution after iodine therapy (Fig. 1).

Postoperatvely the patient began to gain weight and to become overly tired, this condition being helped by the administration of 1 grain (60 mg.) of thyroid daily. The sweating and palpation were appreciably lessened. Preoperatively an electrocardiogram and electroencephalogram were interpreted as verifying the diagnosis of (1) coronary heart disease and (2) epileptic diathesis (Dr. F. A. Gibbs). Appropriate therapy was given for these two conditions, with satisfactory palliative results.

*Comment.*—This patient had hyperthyroidism without hypermetabolism, the fact that a patient with hyperthyroidism can have a normal basal metabolic rate being nothing unusual. To explain the phenomenon it has been postulated that these persons normally have a minus basal metabolic rate determination and that the advent of hyperthyroidism raises it sufficiently so that the basal metabolic rate is then within normal limits. A large series of cases of this type were reported by Werner and Hamilton in 1951.[6]

Although some of the symptoms of hyperthyroidism were present in this patient, how much was produced by the thyroid was open to question. The fact that the

6. Werner, S. C., and Hamilton, H.: Hyperthyroidism Without Apparent Hypermetabolism, J. A. M. A. **146**:450, 1951.

patient had an epileptic diathesis and coronary heart disease clouded the issue. The only positive signs were the enlarged thyroid and a loss of 10 lb. in the previous year.[7]

Therefore, unlike some of Werner and Hamilton's cases, it is not correct to say that this patient had enough positive symptoms and signs to make a diagnosis of

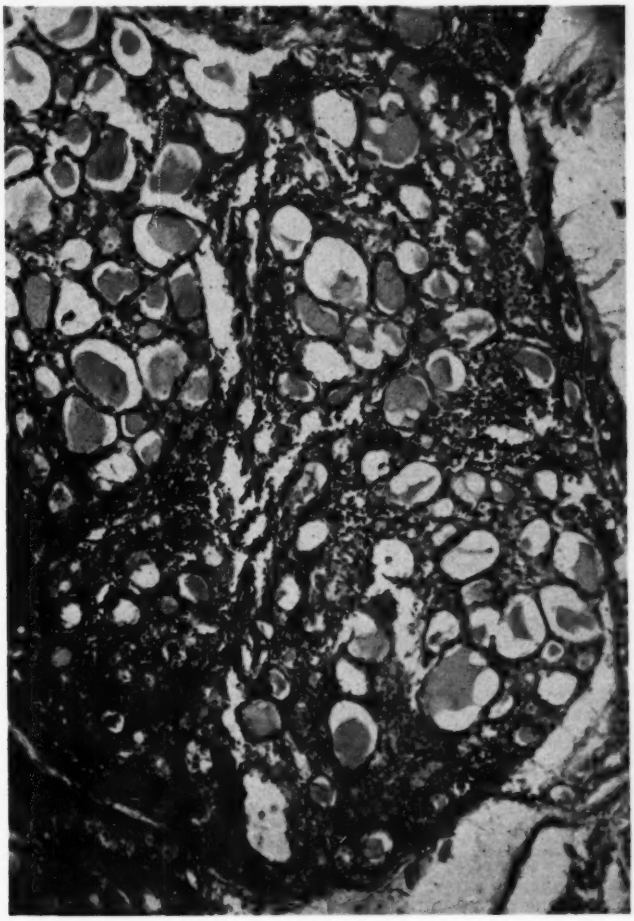

Fig. 1 (Case 2).—Photomicrograph of diffuse parenchymatous goiter (showing marked involution after iodine therapy). Alveoli of the thyroid gland are variable in size, and stroma is increased. Many of alveoli are empty, while others contain small amounts of colloid. Throughout stroma are numerous collections of lymphocytes, sometimes forming mollicles. Lining epithelium of alveoli is of low cuboidal or flattened type.

hyperthyroidism without hypermetabolism. It required a correlation of four factors to make the final diagnosis: (1) positive radioiodine tracer test, (2) normal basal metabolic rate, (3) positive histological evidence, and (4) improvement after surgery.

7. Baumeister, C. F.: Puzzling Causes of Weight Loss, GP **2**:29, 1950.

In one of the patients in this group the radioiodine tracer test was borderline. Fortunately, the histological studies showed a toxic gland and there was proper postoperative improvement. This was in interesting contrast to Case 1, in which the patient was definitely not hyperthyroid and yet had such positive radioiodine tracer studies.

After due consideration it does not seem that a diagnosis of hyperthyroidism, especially hyperthyroidism without hypermetabolism, can be accepted finally in any puzzling situation without a microscopic section from the thyroid of the patient in question. The idea of thyroid biopsy becoming commonplace may seem a little startling at first. However, with the advent of definitive and potentially dangerous medical methods of treating hyperthyroidism (radioiodine, propylthiouracil), it appears more advisable than ever.

Even a positive biopsy does not mean that the patient has hyperthyroidism, as will be seen in Case 3 of this paper. However, if the work-up of a possible case of hyperthyroidism includes three factors (1) thyroid biopsy, (2) basal metabolic rate determination and (3) radioiodine tracer test, a much more intelligent appraisal of the situation can be obtained. This type of analysis is not beyond practicable realization for the majority of persons in the United States, from a geographic and economic standpoint, if the diagnosis of hyperthyroidism is not absolutely clear cut.

CASE 3.—Mrs. H. H., a 46-year-old housewife, was first seen on July 6, 1950. For the past year she had been having attacks of "swelling." This would seem to affect the entire body but was most noticeable in the face and legs. It would be accompanied by a temporary weight gain up to 10 lb. In addition, she had nervousness, fatigue, and sweating, which were of almost life-long duration. She had an extremely good appetite and had gained 15 lb. (6.8 kg.) in the last year.

On examination the patient had warm wet palms. The eyes were somewhat prominent. The thyroid gland was one and one-half times normal size.

Laboratory examination showed a basal metabolic rate of —18%, which verified previous tests that had been made on the patient. The radioiodine test was positive (pick-up 63.2%, urinry excretion 37.8%, total 101%). The patient was given iodine for 10 days preoperatively. On July 28, 1950, approximately 10 gm. of thyroid tissue was removed, leaving about one-fourth of the gland. Histological examination showed a diffuse parenchymatous goiter with involution after iodine therapy (Fig. 2).

Postoperatively the patient gained 10.5 lb. (4.7 kg.) and had hard, edematous, subcutaneous tissue. The thyroid enlarged, and she felt extremely nervous and tired. Diuretics were of only temporary help. However, after eight weeks of therapy, with the administration of 2 grains (0.12 gm.) of thyroid daily, she lost 28 lb. (12.7 kg.). The edema disappeared, the thyroid diminished in size, and the patient felt so much better that she was almost euphoric.

*Comment.*—This patient obviously did not have Graves's disease, in spite of the histological structure of the thyroid. Although she was treated surgically, it was probably unnecessary since her thyroid did not have any of the supertoxic, almost malignant, appearance that is seen in some of the patients with this type of syndrome. Eventually it was necessary to use thyroid in her treatment, which is the only therapy that has been used by me in apparently similar cases.

These patients possibly have intense stimulation of their thyroid glands with excessive amounts of thyrotropic hormone.[8] The administration of thyrotrotopic hormone has no effect on the turnover of iodide of these glands (in contrast with

8. Baker, M. P., and Stanbury, J. B.: An Unusual Goiter in a Young Woman: Normal Thyroid Function with Very High Uptake of Radioactive Iodine, Am. Pract. **2**:804, 1951.

patients with thyrotoxicosis). In some of them there is such intense hyperplasia that a picture almost simulating cancer is seen. Of course, in the patients whose glands show this extreme hyperplasia, complete removal is probably the safest course of action.

Fig. 2 (Case 3).—Photomicrograph of diffuse parenchymatous goiter (showing histologic evidence of involution after iodine therapy). Follicles are of small or medium size and are lined by cuboidal or flattened epithelium. Stroma is increased. Throughout stroma are numerous large collections of lymphocytes, many forming follicles with large germinal centers.

It would be thought that the thyroid had grown to compensate for an iodine deficiency in a patient, in an attempt to make the patient euthyroid. However, experimental work has shown that we are not dealing with a deficiency of iodine supply, nor are we dealing with an inability of the thyroid to extract iodine from the blood stream.

The basal metabolic rate may be normal or it may be rather low. This, of course, may depend on the amount of compensatory hyperplasia of the thyroid. In Stanbury's case, the thyroid was intensely hyperplastic and the basal metabolic rate was normal. In this case the degree of hyperplasia was not so marked and the basal metabolic rate was low.

Previously, it has been thought that with myxedema in a patient who has a goiter, the goiters are colloid (fibrosis and cystic degeneration with a few normal or seminormal follicles). These patients were given enough thyroid extract to hold down the size of the gland. Now it is known that some of these patients, as in hypothyroid children, have iodine-hungry, hyperplastic thyroids, and it will be of great interest to reevaluate them.

CASE 4.—Mr. H. S., a 48-year-old statistical engineer, was first seen in June, 1951. His complaints were numerous but fell mainly into the following three groups: 1. He had been told that he had coronary heart disease, having had shortness of breath with the slightest exertion for the last year. An electrocardiogram taken in June, 1950, was read as showing flattened T waves, and a second one taken in January, 1951, was interpreted as being the same. 2. He suffered from great nervousness and exhaustion. 3. He had a great deal of gastrointestinal trouble, which would vary with his degree of nervousness. In periods of relapse he would have soft to liquid bowel movements with much gas four or five times daily. In addition, he would have much gagging and coughing when he tried to eat, especially in the mornings.

On examination the patient's blood pressure was 139/80 and the pulse rate 96. He was underweight (132 lb. [59.9 kg.] and 68 in. [172.7 cm.] in height) but had been for some years. The eyes were moderately prominent, but the thyroid was apparently not enlarged. The palms were hot and moist, and there was a 3 + fine tremor of the hands.

The basal metabolic rate was + 17%. The radioiodine tracer test was normal (pick-up 44%, urinary excretion 43.5%). The electrocardiograms were interpreted as showing good evidence of old posterior coronary damage.

A diagnosis was made of (1) coronary heart disease and (2) alcoholism with gastritis and anxiety syndrome.

During the next year the patient drank steadily every day and would go on sprees besides. He would get severe Streptococcus sore throats and acute gastritis and have to be hospitalized (four times between February and June, 1952). His weight fell to 115 lb. (52.2 kg.).

The family finally expressed a desire to have him sent to another clinic, which was done in June, 1952. The basal metabolic rate determinations[9] were + 28%, + 18%, and + 23%. Protein-bound iodine was 3.7 γ per 100 cc. The radioiodine tracer test showed nothing abnormal (22.3% pick-up, 67.6% urinary excretion). It was suspected that the patient had Graves's disease, and he was given strong iodine solution U. S. P. for three weeks The basal metabolic rate was then + 14%, and he felt a little stronger. On July 29, approximately 12 gm. of thyroid tissue was removed, about one-fourth of a normal-sized lobe being left on either side. The histological findings were thought to be those of parenchymatous hypertrophy. However, when other expert opinions concerning the slides were obtained, it was felt that this could not definitely be called a toxic thyroid (Fig. 3).

The patient was seen by me on Sept. 27, 1952, about eight weeks after surgery. His basal metabolic rate was + 6%. The blood pressure was 152/100, being reduced by rest to 122/80. The patient looked very much better, having gained 21.5 lb. (9.7 kg.) in weight. He had lost his tremor but still had excessive perspiration. His stomach was not bothering him, and he denied drinking.

However, on Oct. 13, he was seen again at his request and was having difficulties. He was highly nervous and unable to sleep. His stomach was bothering him, his eyes were tearing, he had cramps in his chest and hands, and he had trouble breathing. He was sent to the other clinic

9. Bruger, M., and Hollander, V. P.: Extrathyroidal Hypermetabolism, Ann. Int. Med. **35**:1260, 1951.

at once. On this occasion the basal metabolic rates were + 26%, + 19%, and + 13%. Serum calcium was normal; plasma cholesterol was 293 mg. per 100 cc. His vocal cords moved normally. For a short time after his return to the clinic he felt better.

The patient was seen again, on Oct. 30, at which time he was highly nervous and unable to sleep more than three hours nightly. He complained of a "stopped up" nose, especially in the

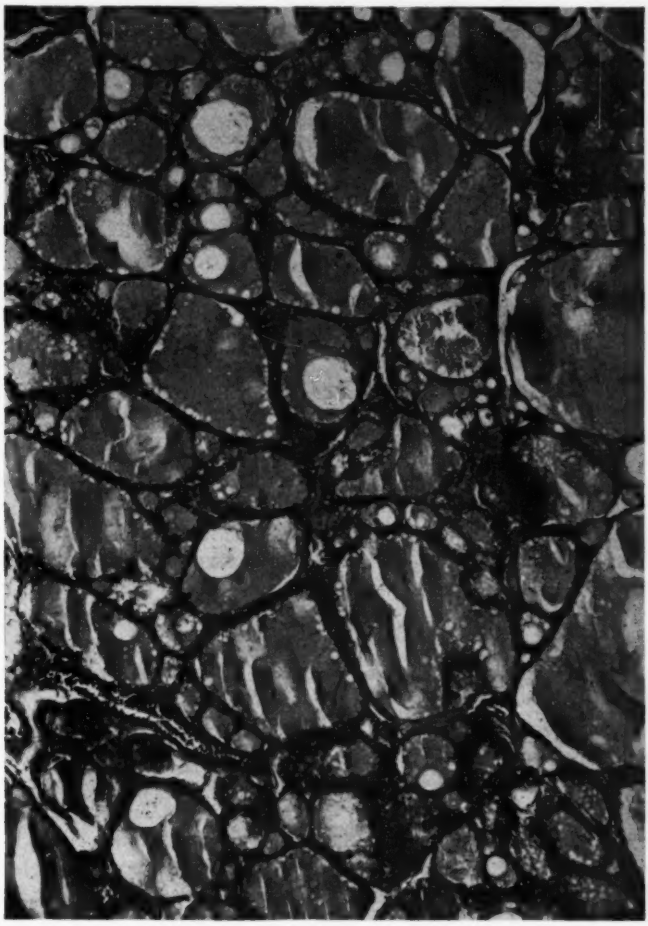

Fig. 3 (Case 4).—Photomicrograph in which most of the microscopic fields are occupied by medium-sized alveoli, only about 10% being taken up by the small ones. Alveoli are lined with low epithelium. Amount of stroma, in the main, is normal, but there is an occasional area showing a slight increase. In these areas there is scant round cell infiltration, without any follicle formation. In this case the histologic diagnosis was in dispute (patient was given iodine therapy).

reclining position, and his nasal mucosa looked swollen and pale. Given suitable nose drops and sedation, he began to improve promptly.

*Comment.*—This alcoholic patient, with a series of essentially normal laboratory tests, is a fine example of the type of patient for whom biopsy should be a "must,"

if any definitive treatment of the thyroid is contemplated. Although an immediate therapeutic success was obtained, it was only temporary, and it is unfortunately true that the most ridiculous types of treatment will often accomplish this result in patients with severe neurosis (as was seen in Case 1). In contrast, and all too often in these persons, the actual cure of an organic disease, such as removal of a calculous gall bladder, will fail to alleviate most of their neurotic symptoms. Patients of the type here represented often have a series of borderline diagnoses made for them, such as chronic brucellosis, chronic amebiasis, or mild hyperthyroidism.

Unfortunately, even if biopsy had been done on this patient, a final diagnosis could not have been made, since several competent observers differed in their interpretation of the micropathology of this gland. There are a number of criteria used in determining toxicity: (1) increase in stroma; (2) degree of round cell infiltration and follicle formation; (3) height of the lining epithelium and amount of infolding and sheet formation, and (4) size of the alveoli. While these rules sound fairly definite, there is often room for much controversy in these borderline cases.

Trying to evaluate the degree of relief in such cases is most difficult, since the neurosis clouds the issue with its mercurial ups and downs. For these reasons it is advisable to tread lightly before doing anything radical in the way of treating a possible hyperthyroidism in one of these patients with a severe neurosis.

## COMMENT

It has been seen that no one test is a reliable indicator of the status of thyroid function in an individual patient, not even a histological study of the gland. It is only by correlating the clinical picture of the patient with the laboratary tests that any conclusions can be drawn. By means of basal metabolic rate determinations, radioiodine tracer studies, and thyroid biopsies, a fairly complete picture can be obtained for practicable clinical purposes. None of these tests is in itself a final answer.

To judge by the clinical picture alone can be grossly misleading, as was shown repeatedly throughout the series. On the one hand, in some cases hyperthyroidism can be masked, and, on the other hand, in some cases neurosis can look very much like Graves's disease.

The basal metabolic rate determinations may be much lower or higher than one would expect. However, they are of value, as in Case 3, in which the low basal metabolic rates and the picture suggestive of myxedema coupled with a high radioiodine pick-up indicated that the patient probably had a hyperplastic gland due to excess thyrotropin. In Case 1, in which the positive symptomatology and the high radioiodine pick-up were opposed by normal basal metabolic rates, major surgery on a normal thyroid gland could have been avoided if the discrepancy had been checked by a biopsy.

The radioiodine tracer test is invaluable as a diagnostic aid but may be very deceiving if used alone. For example, the test was unexplainably and consistently high in Case 1, in which the patient had a normal thyroid. On the other hand, in Case 2, in which the patient had unquestioned hyperthyroidism, the radioiodine test was only borderline. In Case 3, the radioiodine test was so much at variance with the clinical picture and the basal metabolic rates that histologic studies of the gland were clearly indicated.

Even histological studies may be misleading in themselves alone. For example, the hyperplastic gland in Case 3 was not due to Graves's disease, but rather to excess thyrotropin. In Case 4, in which the patient was obviously suffering from severe neurosis, it was difficult to get an agreement on the histological diagnosis from experienced men. However, it is certain that biopsy studies are most desirable and are of particular value in any case in which neurosis is strongly suspected or in which the diagnosis is not clear.

It must be remembered that not all the troubles of a patient may be resolved by the resection of a questionable or slightly toxic gland, especially if there is a severe neurosis. In addition, patients with fairly toxic thyroids may suffer from other organic diseases, some of which may mimic portions of the picture of hyperthyroidism. Therefore a complete evaluation of the case of possible hyperthyroidism enables the physician to know how much relief the patient can reasonably be expected to obtain by various therapeutic maneuvers.

## CONCLUSIONS

Taken by themselves in the diagnosis and treatment of thyroid disease, the clinical picture, basal metabolic rate, radioiodine tracer test, and histological study of the gland may be grossly misleading. When they are correlated, a reasonably good evaluation of a patient can usually be made from a practicable clinical standpoint.

Dr. Granville Bennett assisted with the micropathology and the legends.

# BILIARY-TRACT SURGERY IN ELDERLY PATIENTS

KNOWLES B. LAWRENCE, M.D.
KEITH MERRILL Jr., M.D.
AND
GORDON ARNOLD, M.D
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A STUDY of 580 consecutive patients operated on for biliary-tract disease at the Massachusetts Memorial Hospitals, Boston, during the years 1944 to 1951, has revealed that 70 of these patients, representing 12% of the total, were 70 or more years of age. This was much higher than the 3.3% of such elderly patients noted in the report of gall-bladder surgery from the same hospital for the years 1924 through 1933 [1] and appears to reflect not only increased longevity but also changing conditions of surgery in the 20-year interval.

Two-thirds of the 70 elderly patients in our series required operation because of involved biliary-tract problems. Such a finding is not surprising, since these old people generally shun elective cholecystectomy and consent to operation chiefly because of persistent pain or more serious manifestations.

The definitely higher incidence of postoperative morbidity noted in these elderly patients appeared to be due both to the severe nature of the biliary-tract disease and to the frequent coincidence of complicating medical conditions, such as cardiovascular and respiratory problems, diabetes, and other diseases.

Table 1 summarizes the conditions encountered and the operations performed on 70 patients over the age of 70 years. A total of 72 operations were performed during the chronologic period covered, since in two cases the common duct had to be explored a second time because of recurrent or overlooked stones. Only one case in which there were no stones was noted in the series, and on microscopic examination the gall bladder showed definite recent chronic cholecystitis. Stones, or evidence of stones, passed from the biliary tract were found in the other 69 patients.

Acute cholecystitis was the clinical and pathologic diagnosis in 14 cases, an incidence of 20%; two gall bladders were found to be perforated at operation, and two others showed focal necrosis verging on perforations of the wall.

Common bile duct problems occurred very frequently in the elderly patients. The duct exploration rate for this series of 70 patients was 50%, and the incidence

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Associate Visiting Surgeon and Instructor in Surgery (Dr. Lawrence); Resident Surgeon (Dr. Merrill), and formerly Assistant Resident Surgeon (Dr. Arnold).

1. Boyd, P. L.: The Operative Mortality of Cholecystitis, New England J. Med. **218**:1045-1050 (June 23) 1938.

of common duct stones actually removed, and a few presumptive ones, in view of the finding of a dilated common bile duct with intraductal sediment, was 37.5% for the series. In only 9 of the 36 common duct explorations performed were the findings negative.

Study of the group of 510 patients under the age of 70 years (Table 2) treated in this hospital during the same period revealed a common duct stone incidence of only 9%, with an exploration rate of 20%. These figures for the group were

TABLE 1.—*Surgery for Gallstone Disease in Seventy Patients Aged Seventy Years or Older*

| Pathology | Patients, No. | Surgical Procedures | Deaths |
|---|---|---|---|
| Acute cholecystitis (with stones) | 14 | Cystostomy (9)<br>Cystectomy (5) | Pulmonary embolism (1) |
| Chronic cholecystitis | | | |
| Without stones | 1 | Cystectomy and choledochostomy (1) | |
| With gall-bladder stones | 23 | Cystectomy only (15)<br>Cystectomy and choledochostomy, negative exploration (8) | Pulmonary embolism (1) |
| With common duct and gall-bladder stones | 18 | Cystostomy and choledochostomy (2) | ? bile peritonitis (1) |
| With common duct stones only | 5 | Cystectomy and choledochostomy (21) | |
| Common duct stones only | 4 (two reoperations) | Choledochostomy (4) | |
| Cancer of gall bladder (with stones) | 2 | Cystectomy (1)<br>Radical resection (1) | |
| Fistula or sinus (stones) | 3 | Removal of stones and cholecystectomy (2)<br>Cholecystectomy (1) | Coronary and cerebral accident (1) |
| Gallstone ileus | 1 | Enterotomy (1) | |
| Common duct stricture | 1 | Plastic repair (1) | |

TABLE 2.—*Biliary-Tract Surgery in Massachusetts Memorial Hospitals*

| | Patients | | Acute Cholecystitis, | Jaundice, | Common Duct Exploration, | Common Duct Stone, | Morbidity, | Mortality, |
|---|---|---|---|---|---|---|---|---|
| | No. | % | % | % | % | % | % | % |
| Under 70 yr. | 513 | 88 | 10 | 14 | 33 | 10 | 12 | 1.1 |
| 70 yr. and older | 70 | 12 | 20 | 22 | 50 | 37 | 27 | 5.7 |
| Total | 583 | .. | 11.3 | 15.4 | 36.3 | 13.7 | 14.2 | 1.7 |

closer to those of the series reported from the Lahey Clinic,[2] where stones were found in 16.8% of the 45.7% of all patients in whom the common duct was explored.

The presence or history of jaundice followed the same general trend, with an incidence of 22% in the patients of 70 or more years but only 14.1% in the younger patients. The correlation between jaundice and the finding of common duct pathology was inconstant, however, since a number of patients with definite clinical jaundice or a history thereof were found on exploration to have ducts that did not contain stones. On the other hand, several patients with definite stones and even with dilated common ducts gave no history of jaundice.

2. Marshall, S. F.: Gallstones—A Surgical Problem, S. Clin. North America **28**:627-632 (June) 1948.

Cancer of the gall bladder was found in two patients, or 3.8%. A diffuse thickening of the gall-bladder wall was the extent of the gross change in one of these patients and this proved to be due to malignant infiltration throughout on microscopic examination. Cholecystectomy only was done on this patient, since at the time carcinoma was not suspected. The cancer in the other case was more extensive, though still technically resectable. This case is included among the other case histories to be described.

There were three instances of nonmalignant fistula due to gallstones. In one of these cases, the fistula passed through the diaphragm, pleural space, and chest wall to the skin surface. The preoperative diagnosis was felt to be chronic empyema following pneumonia, with symptoms of two years' duration. There had been no suspicion of gallstone disease. At operation a portion of the 10th rib was removed, a fistulous connection with the gall bladder was demonstrated, and several stones were removed. Recovery was satisfactory, although there was still some bile drainage at the time the patient was discharged from the hospital. The other two fistulas were internal in type. In one case the fistula connected the fundus of the gall bladder with the prepyloric region of the stomach, and a large gallstone was found impacted in this tract. Because of the advanced age of the patient, her poor condition in general, and the degree of local inflammation, surgery was restricted to the removal of the stone and T-tube drainage of the fistula. This patient did well initially but later died of a combination of coronary and cerebral vascular accidents after a long hospital course. A biliary fistula was found in a third case, in which a large stone causing obstruction had been removed from the ileum three years previously. Thereafter this patient had had persistent right upper quadrant pain and other symptoms, and at operation an opening was found between the duodenum and gall bladder. It was closed successfully after the removal of the stone-containing gall bladder.

Another interesting inflammatory complication of common duct stone was one case of pancreatic abscess. This abscess was almost 3 cm. in diameter, contained thick pus, and appeared to be secondary to a stone impacted in the ampulla of Vater.

Actual gallstone ileus was encountered just once in the series and seems of sufficient interest to discuss in the case history section.

## REPORT OF CASES

The following case reports are representative of the many difficult problems encountered in caring for these elderly patients.

CASE 1.—Mrs. S. S., aged 75, was admitted to the Massachusetts Memorial Hospitals in July, 1946.

Eight years previously this patient had had a cholecystostomy at another hospital, with the removal of stones. One year prior to this admission, recurrent attacks of upper abdominal pain with indigestion developed. There was no history of jaundice. A Graham series revealed nonfunctioning of the gall bladder without opaque stones. At operation a chronically inflamed and shrunken gall bladder containing one stone was removed. Another similar stone of mixed type and some calcareous débris was removed from the common duct. It was also necessary to do a transduodenal dilation of the ampulla of Vater, since the probe could not be passed through from above. A T-tube was inserted, and postoperatively on about the 10th day, a cholangiogram showed what appeared to be a normal duct and no evidence of retained stones. The tube was removed.

Two months postoperatively recurrent attacks of pain developed with jaundice. Symptoms continued despite medical biliary flush. Reoperation was done in February, 1947, at which time a soft amorphous-type pigment stone was found and removed from the common duct and the ampulla was dilated. A cholangiogram made after this operation showed some narrowing of the lower end of the common duct at the pancreatic portion. The T-tube was left in for several months to permit intermittent drainage, and after its removal the patient continued to good health.

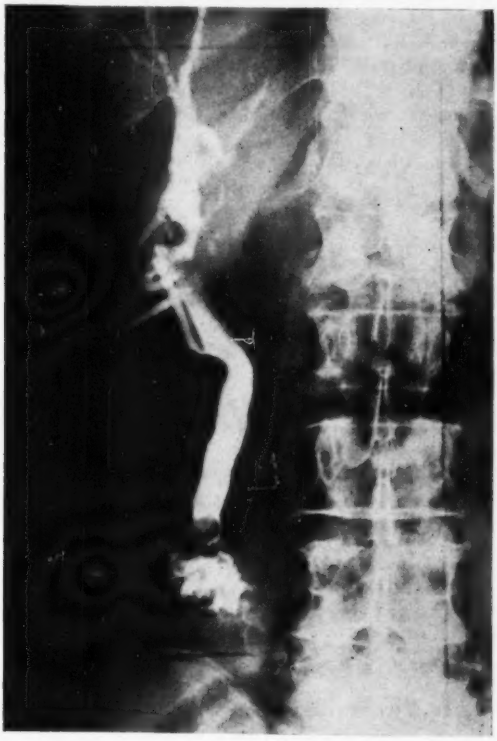

Fig. 1 (Case 2).—Postoperative cholangiogram clearly demonstrating a filling defect at lower end of common bile duct, which, however, is not obstructing flow of bile into the duodenum.

It seems likely that bile stasis due to stenosis following localized pancreatitis and the trauma of transduodenal dilatation was the chief factor in the formation of this soft pigment concretion in the common duct.

Case 2.—Mrs. S. R., aged 73, was admitted to the Massachusetts Memorial Hospitals in September, 1945, complaining of attacks of upper abdominal pain and jaundice of six months' duration. In the hospital it was found that the area over the gall-bladder region was extremely tender. She was definitely jaundiced. Studies indicated that this condition was obstructive in type, but liver function did not show serious impairment. At operation a stone was found in the cystic duct, and several stones and sediment were present in the common duct. The gall bladder was removed and the common duct drained with a T-tube. A postoperative cholangiogram showed a shadow suggestive of stone (Fig. 1). The tube was kept in therefore, and the patient

was admitted to another hospital one month later. A repeat cholangiogram again showed the same negative shadow, and at operation several amorphous pigment-type stones were found in the common duct and removed. The postoperative cholangiogram this time revealed nothing abnormal and the T-tube was removed.

A follow-up history by letter reveals that in this patient recurrent jaundice and pain developed within a few months, and she became critically ill. Her history would suggest that the amorphous calculi reappearing repeatedly in the common duct may have been due to their formation in the intrahepatic biliary tract. The x-ray findings of some calcific foci overlying the liver shadow was also suggestive of this supposition, as was the observation that during the short time that the T-tube was clamped during the second hospital admission it became blocked with calcareous sediment. This tendency of calculi to form in some patients, perhaps due to stasis, within the intrahepatic ducts is occasionally seen.

Case 3.—Mrs. I. J., aged 78, entered the Massachusetts Memorial Hospitals in November, 1949, complaining of recurrent attacks of abdominal pain with vomiting during the previous four to five months. The present attack had lasted two days, and the vomitus had rapidly changed from ingested food to a dark-brown fluid with a fecal odor. She gave a definite history of a gall-bladder attack some 20 to 30 years previously. The patient appeared to be emaciated, dehydrated, and toxic. The nonprotein nitrogen was 61 mg. per 100 cc. The blood chlorides were 88.4 mEq. per liter. A flat x-ray film of the abdomen showed no opacities in the right upper quadrant but did reveal a typical pattern of small bowel obstruction throughout the abdomen. A Harris tube passed into the small bowel largely relieved the distention and permitted improvement in the fluid electrolyte state. A small amount of barium injected through the tube then demonstrated in x-ray a complete obstruction of the ileum in the midpelvic region and also a small crescent of calcific density in this region, which was thought possibly due to a gallstone obstructing the bowel (Fig. 2).

At operation a large oval gallstone measuring nearly 5 cm. in greatest diameter was found to be completely obstructing the lower ileum and was removed without difficulty through a longitudinal incision followed by simple transverse closure of the bowel. This patient made an excellent recovery so far as her abdomen was concerned, but convalescence was prolonged by an infected hypodermatoclysis wound of the thigh.

*Comment.*—This case was the one instance in this series of obstruction of the intestine by gallstone, although in one other case, classified as only a fistula (in this current series), a similar obstructing stone had been removed from the ileum some years before.

Case 4.—Mrs. J. D., aged 74, was admitted to Massachusetts Memorial Hospitals in October, 1949, with a complaint of right upper quadrant pain of eight days' duration. Her history included also progressive weakness, weight loss of 40 to 50 lb. (18 to 22 kg.), and upper abdominal distress, particularly after eating, during the past year. Jaundice and chills and fever had also developed five days prior to admission. She recalled an attack of gallstone colic 12 years previously.

Physical examination revealed definite jaundice and a palpable liver edge without discrete masses. A flat x-ray film showed calcifications suggesting stones in the right upper quadrant of the abdomen. An upper gastrointestinal series demonstrated a fistula between the prepyloric portion of the stomach and a definitely dilated biliary tree. Barium enema revealed another fistulous connection between the colon and the biliary tree.

At operation a hard mass nearly 8 cm. in diameter was found in the region of the gall bladder, replacing it and densely adherent to both the prepyloric region of the stomach and to the transverse colon. Frozen section revealed adenocarcinoma. Further examination disclosed that although there was apparent infiltration of the liver with tumor to the depth of about 1 cm. no distant metastases could be demonstrated in the liver or in the regional nodes. Furthermore, the cystic and common duct regions seemed to be uninvolved. The colon was first divided on either side of the lesion and the stomach divided through its distal third with removal of the first portion of the duodenum. It was then possible to isolate the cystic and common ducts. The

gall bladder was considerably dilated, but, after the common duct was opened, probe and catheter were readily passed through the papilla into the duodenum. No stones could be located at this time. The entire tumor mass and a margin of normal liver from the right lobe were removed with the actual cautery at the line of excision after multiple mattress sutures of absorbable surgical (gut) suture material were placed through the liver substance. The liver bed after the removal of tumor was then deeply cauterized so that a margin of perhaps 3 cm. of tissue was removed or destroyed around the tumor. The operation was completed with an end-to-end anastomosis of the transverse colon and a Billroth I gastroduodenostomy. Operative recovery was uneventful, but, because of the likelihood that stones may have been left behind in the

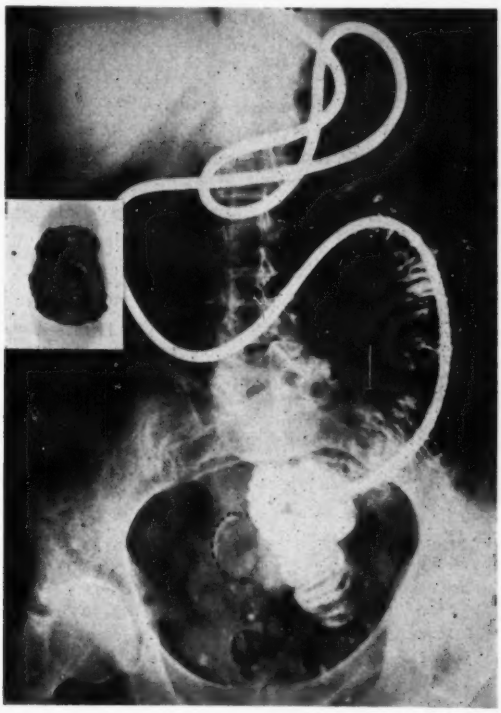

Fig. 2 (Case 3).—Demonstration of gallstone ileus. Barium injected through a Harris tube outlines the dilated small intestine proximal to the obstructing stone, photograph of which is shown in insert.

common duct, as suggested in the postoperative cholangiogram, the patient was discharged with her T-tube in place. About five months later this T-tube pulled out accidentally, followed by the development of jaundice and fatal liver failure due to calculus obstruction of the common duct.

Autopsy revealed that although the site of the excision of the gall-bladder carcinoma was well healed, there were many tumor metastases throughout the liver.

*Comment.*—This case illustrates the usual outcome in cases of well-developed carcinoma of the gall bladder in which the primary disease is removed by extensive surgery. Recurrence or metastatic spread of carcinoma usually occurs rapidly, and life is rarely prolonged by such a procedure.

### MORBIDITY AND MORTALITY

Minor complications such as local wound infections, focal pulmonary atelectasis, and superficial phlebitis occurred rather frequently. More serious complications, cardiorespiratory, in most cases, occurred in 20 patients, or 27%. There were four deaths which had to be classed as operative (Table 1). Two of these were due to massive pulmonary embolism and occurred in 1944, when less vigorous attention was being given to this problem. These patients received no special prophylactic treatment. The third death resulted from a combination of coronary and cerebral vascular accidents. The fourth death was thought, on a clinical basis, to have been caused by bile peritonitis, although an autopsy could not be obtained. It seems rather interesting and significant that there were no deaths from pneumonia or atelectasis in these elderly patients. It is our conviction that the diligent use of antibacterial therapy, modern anesthesia, antibiotic therapy, and early ambulation have largely neutralized the threat of pulmonary infections. Careful attention to liver function, with the administration of adequate dextrose, protein, and vitamins, the prevention of shock with blood transfusions, and the control of infection, as suggested above and by other authors,[3] apparently played an important part in preventing liver failure.

The mortality rate in this series of 70 elderly patients who were treated during the years 1944 to 1951 was 5.7%, whereas the operative mortality for the 35 patients over the age of 70 undergoing biliary surgery in this same hospital during the years 1924 to 1933 was reported as about 35% by Boyd.[1] Gaster's [4] series covering the years 1945 to 1950 in a California hospital included four deaths, a mortality of 16.6% for the 24 cases of biliary-tract surgery in patients over 70 years old. Best,[5] in 1941, also confirmed this finding of a relatively increased mortality in elderly patients requiring surgery for acute cholecystitis. He reported a 16.6% mortality rate for patients over 60 years of age, whereas for those under that age it was only 4%.

In contrast, the mortality rate for the group of 513 patients under the age of 70 years in the balance of our contemporary series was only 1.1% and for all patients of all ages, 1.7%, which is close to the current mortality figures from a large clinic.[6]

### COMMENT

The formidable array of complicated biliary-tract disease problems encountered in elderly patients constitutes a strong argument for elective cholecystectomy earlier in the course of the disease. A review of the histories of the elderly patients suggests that the gallstones, which represent the crux of the problem, have been present and often associated with bouts of cholecystitis for many years.[7] The interesting

3. Glenn, F., and Hays, D. M.: The Causes of Death Following Biliary Tract Surgery for Nonmalignant Diseases, Surg., Gynec. & Obst. **94**:283-296 (March) 1952.

4. Gaster, J.: Surgery of the Biliary Tract: A 5 Year Survey, Arch. Surg. **60**:21-30 (Jan.) 1950.

5. Best, R. R.: The Acute Gall Bladder, Surg., Gynec. & Obst. **73**:312-319 (Sept.) 1941.

6. Priestley, J. T.; Walters, W.; Gray, H. K., and Waugh, J. M.: Annual Report on Surgery of the Biliary System and Pancreas for 1950, Proc. Staff Meet., Mayo Clin. **26**:505-513 (Dec. 19) 1951.

7. Halpert, B., and Lawrence, K. B.: Cholecystitis with Cholelithiasis: A Clinicopathological Study of 60 Patients, Surg., Gynec. & Obst. **62**:43-49 (Jan.) 1936.

studies of Jaguttis [8] and Comfort and his associates [9] offer statistical proof of the considerable tendency of originally "silent gallstones" to become symptomatic and to cause serious biliary-tract complications (Table 3).

Comfort's paper, in 1948, reported on a series of 112 patients known to have gallstones, originally asymptomatic, who had been followed for intervals of 10 to 20 years. He found that in 51, or 46%, symptoms developed later. Twenty-one of these patients required operation and there were three operative deaths. Jaguttis's report, 22 years earlier in the German literature, showed a similar percentage of patients requiring operation but a much higher total mortality of 24% due to gallstones, including five cases of carcinoma of the gall bladder.

TABLE 3.—*Follow-Up in Symptomless Patients with Gallstone*

| Author | Total Patients, No. | Patients with Later Symptoms, No. | Operation Performed | Mortality | | Patients with Carcinoma of Gall Bladder, No. |
|---|---|---|---|---|---|---|
| | | | | No. | Cause | |
| Comfort (Mayo Clinic, 1948)..... | 112 (10-20 yr.) | 51 | 21 | 3 | Pulmonary embolism<br>Subphrenic abscess<br>Bile peritonitis | 0 |
| Jaguttis (Germany, 1926)..... | 114 (10-25 yr.) | .. | 25 | 27 | Operative (14)<br>Other deaths from gallstone disease (13) | 5 |

## SUMMARY AND CONCLUSIONS

A review of the surgery performed for biliary-tract disease at the Massachusetts Memorial Hospitals, Boston, in recent years disclosed a relatively high incidence of patients in the group aged 70 years or older. Such patients also presented a greater number of complications of gallstone disease than did the younger patients in a total series numbering 580 patients during the 1944 to 1951 period.

Postoperative morbidity was much higher in the older patients also, and the mortality rate of 5.7% was in contrast with the 1.1% rate for those patients under the age of 70.

A long history of previous attacks of biliary colic and other symptoms in many of the elderly patients suggests that stones had been there for a long time.

These statistical and clinical findings suggest that elective cholecystectomy years earlier would have saved these patients a great deal of suffering as well as reduced the mortality associated with operative procedures at their more advanced ages.

8. Jaguttis, P.: Mitt. Grenzgeb. Med. u. Chir. **39**:244-269, 1946.

9. Comfort, M. W.; Gray, H. K., and Wilson, J. M.: The Silent Gallstone: A 10 to 20 Year Follow-Up Study of 112 Cases, Ann. Surg. **128**:931-937 (Nov.) 1948.

# FAMILIAL PHEOCHROMOCYTOMA

## Report on Three Siblings with Bilateral Tumors

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THE FIRST successful diagnosis and surgical removal of pheochromocytomas from both adrenal glands of two members of the same family were reported by Calkins and Howard [1] in 1947 and Colston [2] in 1948. The tumors on each side were removed from each of these two patients at different operations, with an interval between the operations in each case.

Calkins and Howard not only diagnosed bilateral pheochromocytomas but pointed out the familial incidence, one of their patients being the niece of the other. Furthermore, the mother of the younger patient, who was also a sister of the elder, probably died of the same condition. In their excellent report Calkins and Howard reviewed the literature from the time of Fränkel,[3] in 1886, who reported the first case, that of a girl 18 years old in whom he found bilateral tumors of the adrenal medulla at necropsy. Calkins and Howard found 15 cases of bilateral pheochromocytoma reported in which the tumors were located in or near the adrenal glands, and 2 cases in each of which tumors arose in Zuckerkandl's body and the retroperitoneal ganglia. No attempt had been made to remove the tumors in any of these cases. Although the clinical information in regard to these patients was far from complete, 7 of the 15 patients were known to have suffered from persistent hypertension. In five cases the tumors were malignant.

At this time we are reporting on the diagnosis and successful removal of bilateral pheochromocytomas from three members of the same family, two sisters and a brother. The father of these three patients died at the age of 42 years from a cerebrovascular accident with a history of attacks suggestive of pheochromocytoma.

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The Regitine used in this investigation was supplied by Ciba Pharmaceutical Products, Inc., Summit, N. J., and the *l*-arterenol, by Winthrop-Stearns, Inc., New York.

From the Section of Physiology (Dr. Roth); Assistant to the Staff, Section of Physiology (Dr. Hightower); from the Division of Medicine (Dr. Barker), and from the Division of Surgery, Mayo Clinic (Dr. Priestley).

1. Calkins, E., and Howard, J. E.: Bilateral Familial Phaeochromocytomata, with Paroxysmal Hypertension: Successful Surgical Removal of Tumors in 2 Cases, with Discussion of Certain Diagnostic Procedures and Physiological Considerations, J. Clin. Endocrinol. **7**:475-492 (July) 1947.

2. Colston, J. A. C.: Surgical Aspects of Bilateral Familial Pheochromocytomata, J. Urol. **59**:1036-1060 (June) 1948.

3. von Fränkel, F.: Ein Fall von doppelseitigem, völlig latent verlaufenem Nebennierentumor und gleichzeitiger Nephritis mit Veränderungen am Circulationsapparat und Retinitis, Virchows Arch. path. Anat. **103**:244-263, 1886.

## REPORT OF CASES

CASE 1.—An 18-year-old girl of Norwegian-English descent was admitted to the Mayo Clinic on Aug. 2, 1951. Her chief complaint was blurring of vision. This was first noticed three weeks previously and had progressed until at the time of admission the patient was unable to read print of ordinary size. The patient had consulted her family physician, who found albumin in the urine and blood pressure of 200/160. Treatment which consisted of rest in bed, sedation, and low-salt diet was without benefit. Approximately one week before admission to the clinic, the patient had noted dull frontal headaches and occasional dull pain in the right costovertebral angle. The tentative diagnosis was malignant hypertension.

Careful questioning revealed that since April, 1951, the patient had been aware of persistent tachycardia and for the past five years she had experienced episodes of palpitation followed by generalized weakness of two to three days' duration. Four months before admission blood pressure had been recorded as normal at the time of a school examination. There was no history of excessive sweating or nervousness. For the past two months she had worked as a clerk in an office.

The medical history was noncontributory. In general, the patient had always enjoyed excellent health. The family history will be discussed later.

Physical examination revealed a pale young woman in no acute distress who had blood pressure of 190 mm. Hg systolic and 150 diastolic in the arms and 178 systolic and 138 diastolic in the legs. The heart was enlarged to the left, and the cardiac tones suggested gallop rhythm. The pulse rate was 124 beats per minute. Examination of the abdomen revealed no abnormal findings. Examination of the optic fundi revealed bilateral papilledema of 3 D. with large exudates and a few hemorrhagic areas near the periphery. The retinal arterioles showed minimal sclerosis but marked focal constrictions. Venous engorgement was prominent. There was some retinal detachment in the inferior temporal quadrant in the right eye.

The results of routine laboratory investigations, including those for hemoglobin, leucocytes, blood urea, and flocculation tests for syphilis, revealed normal conditions. Roentgenologic examination of the thorax and an excretory urogram were reported as noncontributory. The electrocardiogram was interpreted as showing sinus tachycardia, with a cardiac rate of 124 per minute. A lengthened Q wave was observed in Leads II and III, and the T wave was notched in Leads I and II and diphasic in Lead III. Urinary excretion of 17-ketosteroids was 1.5 mg. per 24 hours and that of corticosteroids was 0.56 mg. per 24 hours. The basal metabolic rate was reported as +6%. On one of two occasions albuminuria, Grade 2 (on a grading basis of 1 to 4), was found on routine urinalysis; otherwise the urinalysis gave negative results.

Rest in bed and sedation had little effect on the blood pressure, which showed considerable fluctuation and varied from 160/130 to 240/190. The standard [4] cold pressor test produced an elevation in blood pressure to 216/166 from a basal level of 190/134.

A piperoxan [5] test for pheochromocytoma was carried out on two occasions. During one, in which 16 mg. was given intravenously, the blood pressure decreased from a basal level of 190/130 to 156/112 in 4.5 minutes after the injection and returned to 190/150 in 10 minutes. On another occasion 20 mg. of piperoxan was given intravenously. This dose produced a decrease in the blood pressure from a basal level of 186/144 to 124/100 in two minutes. At the end of 10 minutes the blood pressure had returned to 184/134.

Phentolamine (Regitine [6]) in a dose of 5 mg., administered intravenously, lowered the blood pressure from a basal level of 190/140 to 118/88 in 2 minutes, and at the end of 10 minutes the blood pressure had returned to 200/140 (Fig. 1*A*). The immediate subsequent rise in the blood pressure following the initial fall was greater than usual. However, the initial rapid decrease in blood pressure is characteristic of a positive result and is indicative of pheochromocytoma.

4. Hines, E. A., Jr., and Brown, G. E.: A Standard Test for Measuring the Variability of Blood Pressure: Its Significance as an Index of the Prehypertensive State, Ann. Int. Med. **7**:209-217 (Aug.) 1933.

5. Goldenberg, M.; Snyder, C. H., and Aranow, H., Jr.: New Test for Hypertension Due to Circulating Epinephrine, J. A. M. A. **135**:971-976 (Dec. 13) 1947.

6. Gifford, R. W., Jr.; Roth, G. M., and Kvale, W. F.: Evaluation of New Adrenolytic Drug (Regitine®) as Test for Pheochromocytoma, J. A. M. A. **149**:1628-1634 (Aug. 30) 1952.

The response of the patient to phentolamine administered intramuscularly and orally also was determined (Fig. 1*B*). On two occasions 5 mg. of phentolamine was administered intramuscularly [7] and produced no significant fall in blood pressure. Thus to avoid such false negative results phentolamine should be given intravenously for diagnostic purposes. Furthermore, 60 mg. of phentolamine was given orally at one time and at another time 20 mg. of piperoxan was administered sublingually, but neither produced a significant fall in blood pressure.

In view of the positive results of the phentolamine and piperoxan tests for pheochromocytoma when the drugs were given intravenously, the relatively short clinical history of severe hypertension in a young woman, and the marked fluctuations in blood pressure, exploratory operation for pheochromocytoma was deemed advisable.

The anesthetic consisted of thiopental (Pentothal) sodium supplemented with curare, nitrous oxide, and oxygen. The upper part of the abdomen was opened through a high anterior, transverse, slightly curved incision. A multilobulated tumor was found in each adrenal gland. The tumor on the right side was approximately 4 cm. in diameter and weighed 35 gm. This was

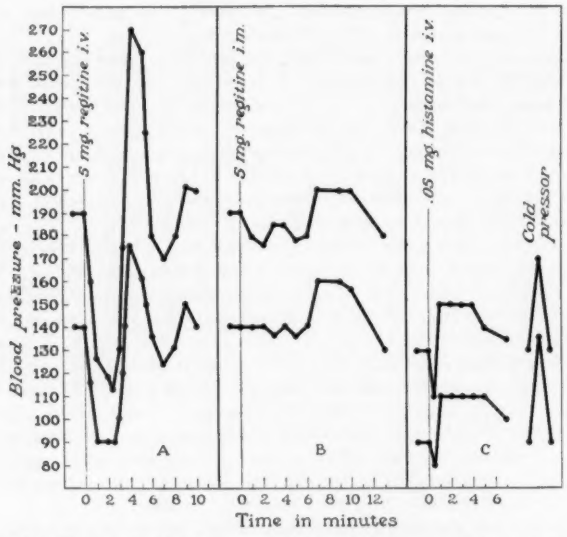


Fig. 1 (Case 1).—Changes in blood pressure before and after operation. *A*, before operation: The sudden rapid fall of the blood pressure after the intravenous injection of 5 mg. of phentolamine is interpreted as a positive result indicative of pheochromocytoma. *B*, before operation: Practically no fall of blood pressure but instead a slight rise accompanied the intramuscular injection of 5 mg. of phentolamine. Results of this test indicate that a pheochromocytoma was not present; in other words, this is a false negative test. *C*, after operation: After the intravenous administration of 0.05 mg. of histamine base in 0.5 ml. of isotonic sodium chloride solution, after the initial fall at 30 seconds, only a slight rise in the blood pressure occurred. The rise of the blood pressure was less than that produced during the cold pressor test.

removed with the capsule intact, with preservation of about a third of a normal-appearing adrenal gland on this side. On the left side the tumor was larger; it was about 5 cm. in diameter and weighed 55 gm. This tumor also was removed intact and a small amount of normal adrenal tissue was preserved on this side. There was nothing to suggest malignant growth in the appearance of either gland, and general abdominal exploration revealed no other significant findings.

7. Emlet, J. R.; Grimson, K. S.; Bell, D. M., and Orgain, E. S.: Use of Piperoxan and Regitine® as Routine Tests in Patients with Hypertension, J. A. M. A. **146**:1383-1386 (Aug. 11) 1951.

Marked elevations of blood pressure which occurred during the operation were satisfactorily controlled by the intravenous administration of piperoxan in doses of 10 mg. Immediately after removal of all tumor tissue the blood pressure became unobtainable and the patient appeared to be in profound shock. The vascular collapse which this patient experienced at this time was readily controlled by the continuous intravenous administration of *l*-arterenol and epinephrine [8] (nor-epinephrine).

Due to the fact that the patient had bilateral pheochromocytomas and that considerable adrenal tissue was removed at the time of operation, 200 mg.[9] of cortisone was given intramuscularly during the operative procedure and 75 ml. (3 mg. of total solids per milliliter) of aqueous adrenal cortex extract was added to the intravenous fluids which were given postoperatively. The patient's blood pressure stabilized at approximately 110/80 under the influence of the postoperative vasopressor therapy, which was discontinued after 27 hours. Intramuscular administration of cortisone was continued in decreasing doses until the third postoperative day. The postoperative course was uneventful, and on the 11th postoperative day a histamine test for pheochromocytoma gave negative results, as shown in Figure 1*C*. Because the blood pressure was so much lower after operation, it was necessary to perform a histamine test rather than a phentolamine test.

The retinitis improved rapidly after operation, and vision returned to normal except for a partial field defect at the site of retinal detachment. The patient was last seen in August, 1952, one year after operation, at which time her blood pressure was 110/68. She appeared to be in excellent health and had had no recurrence of symptoms. A histamine [10] test for pheochromocytoma at this time gave negative results.

During the course of obtaining a detailed history from the first patient (Case 1), the question of excessive sweating was raised. Although the patient had not experienced this symptom herself, she remarked, "If you want to see somebody sweat, you should see my sister." She also stated that her sister had high blood pressure. When it was discovered that this patient had bilateral pheochromocytomas, the statement she had made concerning her sister was recalled and we suspected a familial occurrence of pheochromocytoma, such as reported by Calkins and Howard.

Case 2.—The second patient was a 28-year-old housewife, a sister of the first patient. She was first seen when she came to visit her sister who had just undergone operation for bilateral pheochromocytomas. On questioning her we found that she had a clinical history even more suggestive of pheochromocytoma than her sister. It was suggested therefore that she submit to examination.

The clinical history revealed that in 1942 this patient had had two sudden severe headaches associated with blackouts and subsequently she had experienced a dull occipital headache of about six months' duration. In 1946, during the last month of the first pregnancy, elevated blood pressure and albuminuria were discovered. At this time the patient began to have sudden severe occipital headaches associated with palpitation, dyspnea, and pallor. The attacks would last 10 to 15 minutes and were associated with persistent hypertension. In 1947 the headaches became less violent but would persist from a few hours to two days. The headaches were frequently associated with marked sweating and sometimes with dyspnea and palpitation. In 1948 a second pregnancy was terminated at seven months with the delivery of a stillborn child. Subsequently the hypertension had become severer and the patient had noticed intermittent mild palpitation and occasional orthopnea. Physical exertion almost always was followed by marked weakness and excessive sweating so that she was unable to do ordinary housework.

8. Hightower, N. C., Jr.; Roth, G. M., and Priestley, J. T.: Operative and Postoperative Control of Blood Pressure in Patients with Pheochromocytoma, Central Soc. Clin. Res. **25**:41-42, 1952.

9. Priestley, J. T.; Sprague, R. G.; Walters, W., and Salassa, R. M.: Subtotal Adrenalectomy for Cushing's Syndrome: A Preliminary Report of 29 Cases, Ann. Surg. **134**:464-472 (Sept.) 1951.

10. Roth, G. M., and Kvale, W. F.: A Tentative Test for Pheochromocytoma, Am. J. M. Sc. **210**:653-660 (Nov.) 1945.

On physical examination the blood pressure was found to be 190/130 and the pulse rate 108. The patient was perspiring freely, although the hands were cold and dry. The heart was slightly enlarged and there was a diffuse apex beat. A loud systolic murmur was audible at the base of the heart and along the left border of the sternum. The lower pole of the right kidney was palpable, but no other significant findings were noted on examination of the abdomen. The retinal arterioles showed a slight degree of sclerosis associated with some general narrowing and focal contrictions. Two cotton-wool patches were observed in each fundus.

Routine laboratory tests, including urinalysis, determination of hemoglobin, erythrocyte count, leucocyte count, differential count, and sedimentation rate, gave results within normal limits. The value for blood urea was 46 mg. per 100 cc., that for blood sugar was 90 mg. per 100 cc., and the Kline flocculation test for syphilis gave negative results. Roentgenographic examination of the thorax revealed no abnormalities. The basal metabolic rate was +48%. The

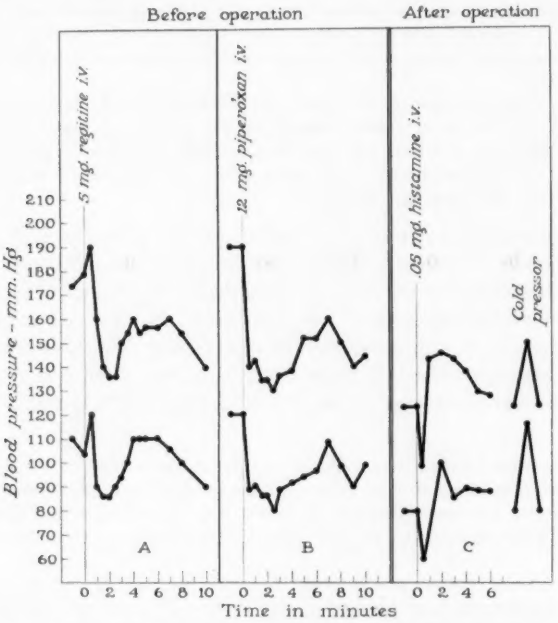


Fig. 2 (Case 2).—Changes in blood pressure before and after operation. *A*, before operation: The sudden rapid fall in blood pressure following intravenous administration of 5 mg. of phentolamine may be interpreted as a positive result indicative of pheochromocytoma. *B*, before operation: Likewise, the sudden rapid fall in blood pressure following intravenous administration of 12 mg. of piperoxan hydrochloride may be interpreted as a positive result indicative of pheochromocytoma. *C*, after operation: After the intravenous administration of 0.05 mg. of histamine in 0.5 ml. of isotonic sodium chloride solution, subsequent to the initial fall at 30 seconds, only a slight rise in blood pressure occurred, which was slightly lower than the response during the cold pressor test.

electrocardiogram was read as showing sinus tachycardia, a cardiac rate of 115, and some slurring of the QRS complex in Leads I and III. A lengthened Q wave was also observed in Leads II and III. An excretory urogram demonstrated downward displacement of the right kidney, but normal function was present in both kidneys.

The standard cold pressor test produced an elevation in the blood pressure of 208/130 from a basal level of 198/128. After the intravenous administration of 5 mg. of phentolamine, the blood pressure decreased from 190/120 to 136/86 (Fig. 2*A*) within 2 minutes, and at the end

of 10 minutes the blood pressure was still only 140/90. Piperoxan hydrochloride also was administered intravenously in a dose of 12 mg.; it decreased the blood pressure from 190/120 to 142/90 in one minute and to 130/84 in two and a half minutes. Ten minutes after the administration of piperoxan the blood pressure was 144/98 (Fig. 2 *B*).

Surgical exploration was advised in view of the positive results of pharmacologic tests for pheochromocytoma and the clinical history suggestive of this lesion. Bilateral tumors were strongly suspected. The abdomen was opened on Aug. 23, 1951, through a high anterior, transverse incision. Bilateral pheochromocytomas were found and removed. Both tumors were lobulated and well encapsulated. The larger tumor, on the right side, weighed 318 gm. and the smaller one, on the left side, 105 gm. Because of the size of the tumors it was apparent that little, if any, adrenal tissue could be preserved on either side. Consequently, 30 ml. of whole adrenal cortex extract was administered intravenously at once and 20 ml. was given intramuscularly. Two hundred milligrams of cortisone also was promptly administered intramuscularly. Immediately after the blood supply of the second tumor was interrupted, a precipitous drop occurred in the blood pressure. This was controlled by continuous intravenous administration of epinephrine and *l*-arterenol. Vasopressor therapy was continued for 48 hours after operation.

The immediate postoperative convalescence was uneventful, and blood pressure remained about 110/80. Cortisone was administered during the first six postoperative days in decreasing doses which ranged from 200 to 25 mg. per day. Although there was considerable doubt that the patient had enough functioning adrenal cortex to prevent adrenal cortex insufficiency, it was decided that administration of cortisone should be discontinued in order to ascertain the status of adrenal function. The patient was observed closely. Seventeen days after operation and 11 days after the last dose of 25 mg. of cortisone, the patient began to complain of easy fatigability, listlessness, and drowsiness. After an afebrile postoperative course, fever (temperature of 101 F.) developed on the 17th postoperative day and the patient complained of pain in the upper part of the abdomen. There had been no nausea, vomiting, hiccup, or loss of appetite, although she had lost 3 lb. (1.4 kg.) during the past four or five days. The blood pressure was 130/100. Fever subsided within 24 hours, and as the patient evidenced no acute distress, corticotropin was given to help determine whether any functioning adrenal cortex tissue remained. Urinary excretion of 17-ketosteroids or corticosteroids did not increase during this period. During the next few days the patient appeared weaker and mild hiccup developed. Electrolyte studies of the blood at this time revealed values for calcium of 12 mg. per 100 cc.; sodium, 126 mEq. per liter; potassium, 6.6 mEq.; carbon-dioxide-combining power, 23 mEq., and chloride, 90 mEq. per liter. As all of these findings suggested adrenal cortex insufficiency, substitution therapy was instituted. It consisted of 6.25 mg. of cortisone given orally four times a day and 2 mg. of desoxycorticosterone acetate given buccally twice a day. The patient immediately experienced a feeling of well-being, and all symptoms of adrenal cortex insufficiency disappeared.

Before her discharge on Sept. 28, 1951, a histamine test was negative for pheochromocytoma (Fig. 2*C*).

The patient continued in good health but did not menstruate, and in February, 1952, she discovered she was four months' pregnant. She continued to take the same dose of cortisone and desoxycorticosterone acetate until the later months of pregnancy, when her physician in her home locality reduced the daily dose of cortisone to 12.5 mg. because of some edema of the legs. This was followed by disappearance of the edema and also by decrease in the concentration of sodium in the serum and the carbon-dioxide-combining power. With the changes in electrolytes, the dose of cortisone was increased to 25 mg. a day. On July 19, 1952, the patient was delivered of a normal baby girl weighing 6 lb. 5 oz. (2,871.5 gm.). During the first three postpartum days the daily dose of cortisone was increased to 100 mg. and then gradually reduced to the original maintenance dose of 25 mg.

Since removal of the bilateral pheochromocytomas the patient's blood pressure has remained normal. When she was last seen by us, on Aug. 25, 1952, the blood pressure was 130/86.

Case 3.—When it was found that both sisters had bilateral pheochromocytomas, an inquiry was made concerning the health of their brother, who was 25 years old and worked as an auto-

mobile mechanic. So far as they knew he did not have hypertension and apparently was in good health, for he had just served three years in the Army. When the brother came to visit his sisters while they were in the hospital, he was advised to undergo examination for possible pheochromocytoma.

The clinical history revealed that for the past six years the patient had had nervous spells which consisted mostly of a mild tremor of the hands associated with weakness and some pallor. These episodes would occur as often as every three days and would last for 10 minutes to 3 hours. He felt that they usually occurred when he was a little excited, emotionally upset, anxious, or self-conscious. He stated that such episodes were particularly likely to occur when he played poker and that the tremor of his hands frequently revealed to his associates the fact that he held good cards. His friends called him "Shakey." He had not noticed headache, excessive sweating, palpitation, or pain in the chest. The patient thought that exercise or physical work gave some relief from the attacks.

The patient was a well-built young man who appeared to be in excellent health. The blood pressure was 150/70 and the pulse rate 72. There was palpable fullness in the right upper part of the abdomen associated with slight tenderness on deep pressure. No definite mass was discernible. Examination of the optic fundi revealed only minimal narrowing of the retinal arterioles. During one of his "nervous spells" the blood pressure was 180/90, and some pallor, particularly about the mouth, was noted.

All of the routine laboratory investigations gave negative or normal results. The basal metabolic rate was —5%. The electrocardiographic tracing was interpreted as showing nothing abnormal; it demonstrated a sinus rhythm, with a cardiac rate of 64 beats a minute. The excretory urogram showed normal conditions.

The standard cold pressor test produced an elevation in blood pressure from a basal level of 120/70 to 140/106. Pharmacologic tests for pheochromocytoma were carried out with histamine, tetraethylammonium chloride,[11] and methacholine chloride (Mecholyl).[12] The patient's response to each was indicative of pheochromocytoma (Fig. 3). When 0.05 mg. of histamine was given intravenously, the blood pressure increased from a basal level of 110/80 to 196/136 (Fig. 3*A*) within two minutes. When 250 mg. of tetraethylammonium chloride was administered intravenously, the blood pressure increased from a basal level of 124/88 to 224/176 in two and a half minutes (Fig. 3*C*). A subcutaneous dose of 12.5 mg. of methacholine chloride produced a similar response (Fig. 3*B*) but not to the same degree as the histamine and tetraethylammonium chloride. The peak response after the dose of methacholine chloride was 160/98 and occurred within four minutes. The basal blood pressure immediately prior to the administration of methacholine was 120/86. Thus in each case the response of the systolic blood pressure following use of histamine, tetraethylammonium chloride, and methacholine exceeded the response to the standard cold pressor test.

Because the patient's two sisters had been found to have bilateral pheochromocytomas and because of a somewhat suggestive clinical history and the positive results of pharmacologic tests for pheochromocytoma, the patient was advised to have surgical exploration, although at this time he was experiencing only minimal symptoms.

As with the other two patients the abdomen was explored through a high anterior, transverse incision. General abdominal exploration was negative except for the adrenal glands. Two distinct tumors were present in the right adrenal gland. These measured approximately 2 and 3 cm. in diameter respectively. Approximately 15 or 20% of a normal adrenal gland remained after their removal. A large multilobulated partially cystic tumor which measured 8 by 6 by 6 cm. was present on the left side. It was necessary to perform complete adrenalectomy on the left side in order to remove this large tumor. When it became apparent that considerable adrenal cortical tissue had to be sacrificed, 200 mg. of cortisone was given at once intramuscularly and additional cortisone was given subsequently in the same manner.

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11. LaDue, J. S.; Murison, P. J., and Pack, G. T.: Use of Tetraethylammonium Bromide as a Diagnostic Test for Pheochromocytoma, abstracted, Am. J. Med. **3**:118 (July) 1947.

12. Guarneri, V., and Evans, J. A.: Pheochromocytoma: Report of a Case, with a New Diagnostic Test, Am. J. Med. **4**:806-813 (June) 1948.

During the operation excessive increases in blood pressure were controlled by the intravenous administration of phentolamine. Immediately after operation and during the first 60 hours after operation, blood pressure was maintained in the neighborhood of 110/70 by use of a combination of epinephrine and *l*-arterenol. This was given continuously by slow intravenous drip. Fluids were administered intravenously through the fourth postoperative day, during which period 9 gm. of sodium chloride was given daily.

Cortisone therapy consisted of intramuscular injections of 100 mg. on the second postoperative day, 50 mg. on the third, and 25 mg. on the fourth and fifth. Then administration of cortisone was discontinued with no subsequent evidence of adrenal cortex insufficiency.

By the fourth postoperative day the blood pressure had stabilized at 120/70, but on the fifth day it rose to 150/90, remained there for 24 hours, and then returned to its former level. This late rise in the blood pressure probably was due to the cortisone.

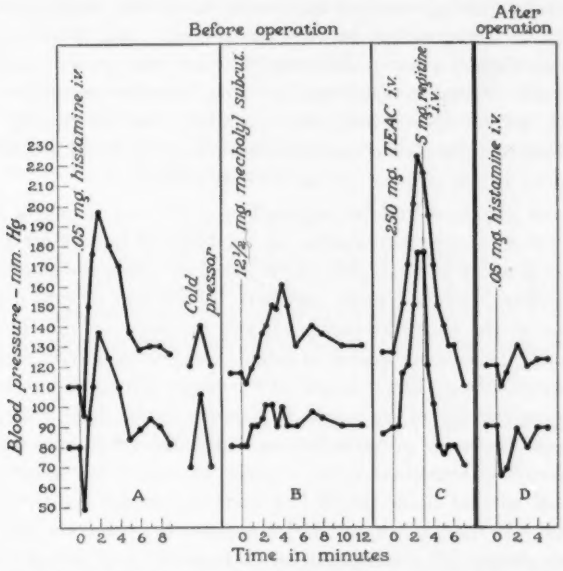


Fig. 3 (Case 3).—Changes in blood pressure before and after operation. *A*, before operation: Changes resulting from immersion of one hand in cold water at 4 C. for one minute and from the intravenous administration of 0.05 mg. of histamine base in 0.5 ml. isotonic sodium chloride solution. *B*, before operation: Changes from the subcutaneous administration of 12.5 mg. of methacholine chloride. *C*, before operation: Changes from intravenous administration of 250 mg. of tetraethylammonium chloride. The rise in blood pressure following all three of these drugs may be interpreted as indicative of pheochromocytoma. After the administration of tetraethylammonium chloride (*C*), because of the severity of the headache 5 mg. of phentolamine was given intravenously. It relieved the headache and produced a sudden rapid fall in blood pressure. *D*, after operation: Changes in blood pressure following the intravenous administration of 0.05 mg. of histamine base in 0.5 ml. of isotonic sodium chloride solution showed the usual decrease in blood pressure 30 seconds after administration of the histamine and the lack of a great increase.

With the exception of mild gastric retention, which developed on the second postoperative day and which was relieved by gastric suction, the patient's convalescence was uneventful. A histamine test carried out nine days after operation gave negative results (Fig. 3*D*). At the time of dismissal, two weeks after operation, the blood pressure was 120/80 and the patient stated that he felt entirely different than he had prior to operation. He particularly noted that he was less nervous.

The patient had continued in good health when last heard from, in July, 1952.

COMMENT

Satisfactory surgical treatment of pheochromocytoma requires that the surgeon be mindful of certain pathologic characteristics of these tumors. While it is true that pheochromocytoma usually is found as a single, encapsulated, benign tumor located in one adrenal gland, exceptions occur in all these respects. In other words, tumors of this type may be multiple, malignant, bilateral, and located elsewhere than in an adrenal gland. Because of the relative infrequency of these tumors, it is difficult to state definitely the exact percentage of cases in which these variations from the usual findings may be encountered. However, they occur with sufficient frequency so that the surgeon should perform an operation for this type of tumor in such a manner that regardless of the findings a satisfactory surgical procedure can be conducted. Although various approaches have been employed to expose the adrenal glands, including posterolumbar, transthoracic and thoracicoabdominal, a high transverse, slightly curved abdominal incision has proved most satisfactory in our experience. Fortunately, the patient who has pheochromocytoma is almost invariably thin, and an approach of this type affords not only ready simultaneous access to both adrenal glands but also permits thorough general abdominal exploration if the tumor is not situated in the adrenal glands.

Both adrenal glands should be explored in every case, as there is no way of being certain prior to operation whether or not bilateral tumors are present. Likewise, search for a tumor in a possible ectopic location within the abdomen should be a routine procedure. These tumors also have been found in rare instances in the thorax or even in the neck. Palpation of, and pressure on, the tumor should be minimized during its removal because of serious vasopressor effects which may result from these manipulations. Blood supply of the tumor should be interrupted as soon as possible during removal of the tumor. It is most unusual that an adequate amount of adrenal tissue cannot be preserved, even when bilateral tumors are present, but care should always be exercised in this regard. In case of any question concerning the adequacy of adrenal tissue which is preserved, prompt substitution therapy is most important. If the patient has had sustained hypertension before operation, blood pressure should fall precipitously after removal of all tumor tissue. If such a drop in pressure does not occur after the removal of a tumor, the presence of additional tumor tissue should be suspected. A pharmacologic test performed at this time with one of the vasodepressant agents, such as phentolamine, may afford valuable additional evidence concerning the persistence of tumor tissue.

It is of interest that from the anatomic and pathologic standpoints the tumors in these three cases were similar, but the clinical manifestations were different. In each case, both adrenal glands were involved and the tumors on each side consisted of multiple nodules. Although the total amount of tumor tissue varied somewhat, being greatest in Case 2 and least in Case 3, the first patient presented the clinical syndrome of fulminating malignant hypertension with severe retinopathy, the second presented the picture of a chronic hypertension of moderate severity with intermittent attacks which were at least suggestive of hyperadrenalism, and the third patient had no hypertension and his symptoms were minimal. It is unlikely that the third patient would have sought medical aid or that the diagnosis would have been made if tumors had not been diagnosed and removed successfully from his two

sisters. It is probable that the father of these three patients died of pheochromocytoma. His history of hypertension with attacks of palpitation, headache, excessive sweating, and weakness was very suggestive of pheochromocytoma.

Our experiences with these three patients emphasize the importance of controlling hyperadrenalism during operations for these tumors and of continued close observation of the patients during the immediate postoperative period with immediate institution of substitution therapy with epinephrine and arterenol any time symptoms of shock developed.

The second patient is of particular interest in that after removal of the tumors there was no remaining cortical adrenal tissue, as far as could be determined at the time of operation. In spite of the fact that the clinical picture of adrenal cortex insufficiency developed subsequently, this was completely controlled by continued therapy with cortisone and desoxycorticosterone acetate. It is of further interest that with the aid of this substitution therapy, this patient subsequently went through a pregnancy and was delivered of a normal child without untoward incident, in spite of the fact that the delivery required manipulation with forceps because of the occipitoposterior position of the child. Such an occurrence has been reported previously in patients with Addison's disease.[13]

## SUMMARY

So far as we know this is the first report of the diagnosis and successful removal of bilateral pheochromocytomas from three members of the same family, two sisters and a brother. Likewise, to the best of our knowledge, there has been no previous report of the successful surgical removal of bilateral pheochromocytomas in a single operation.

13. Jailer, J. W., and Knowlton, A. I.: Simulated Adreno-Cortical Activity During Pregnancy in an Addisonian Patient, J. Clin. Invest. **29**:1430-1436 (Nov.) 1950.

# CYSTS ABOUT THE PERICARDIUM

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SINCE 1934, when Pickhardt [1] first reported the successful removal of a pleuro-pericardial cyst from the mediastinum, numerous reports have appeared in the literature on the subject of thin-walled cysts formed in close relationship to the pericardium, often in the costophrenic angle or high in the mediastinum. Characteristically, these cysts are filled with clear watery fluid and are lined by mesothelium or endothelial-like cells. Two recent contributions to this subject by Drash and Hyer,[2] and Lillie, McDonald, and Clagett,[3] of the Mayo Clinic, include opinions not only as to the origin of these cysts in relation to the embryological development of the pericardium, but also reviews of previously reported cases as well as the clinical features and pathology of their own series. Because of the rarity of these mediastinal cysts, although it is possible that many of the cases have not been reported, it seemed justifiable to record our experience with two patients who had been observed with masses in the mediastinum which at operation proved to be cysts lying adjacent to the pericardium.

## REPORT OF CASES

CASE 1.—F. M., a 46-year-old single white woman, was admitted to the Presbyterian Hospital, Chicago, on Feb. 25, 1945. The chief complaint concerned a tumor mass in the chest, known to be present since April, 1944. She had experienced progressive pain to the right of the midsternum deep in the chest for approximately four to five years. The pain radiated through to the back and up into the neck. There was no history of cough, dyspnea, hemoptysis, or pulmonary infection. Previous surgery included thyroidectomy, cholecystectomy, appendectomy, abdominal hysterectomy, oophorectomy, and hemorrhoidectomy.

In 1944 roentgenograms of the chest showed the heart shadow within normal limits. There was a rounded area of increased density at the level of the hilus of the right lung, suggesting an aneurysm. Fluoroscopic examination of the thorax demonstrated a pulsating tumor in the anterior mediastinum on the right which was described as an aneurysm of the ascending aorta.

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‡ Memorial Hospital, New York.

1. Pickhardt, O. C.: Pleuro-Diaphragmatic Cyst, Ann. Surg. **99**:814, 1934.

2. Drash, E. C., and Hyer, H. J.: Mesothelial Mediastinal Cysts: Pericardial Celomic Cysts of Lambert, J. Thoracic Surg. **19**:755, 1950.

3. Lillie, W. I.; McDonald, J. R., and Clagett, O. T.: Pericardial Celomic Cysts and Pericardial Diverticula, J. Thoracic Surg. **20**:494, 1950.

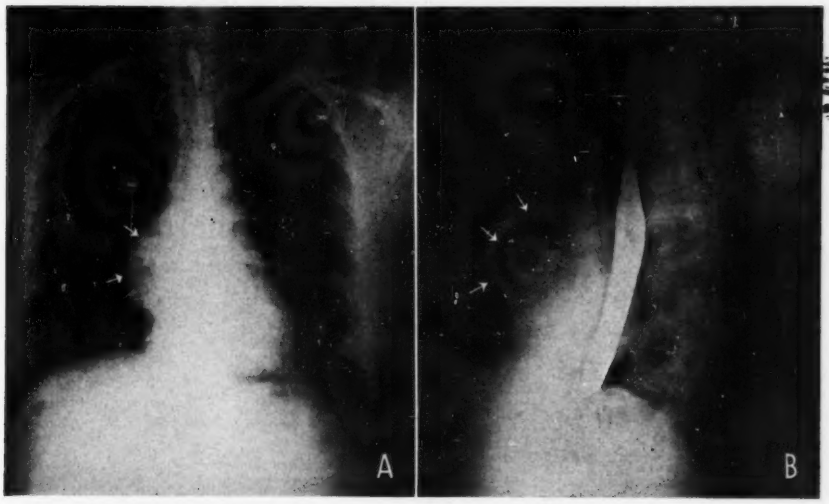


Fig. 1.—*A*, roentgenogram of chest, demonstrating oval-shaped tumor arising from right side of mediastinum. *B*, oblique view of same lesion, showing more clearly relationship of cyst to pericardium.

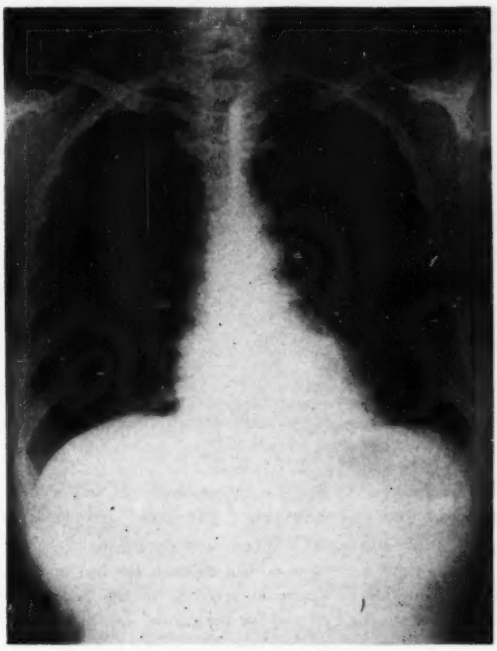

Fig. 2.—X-ray appearance of operative site two weeks after removal of pericardial cyst.

In 1945 physical examination revealed nothing unusual in the chest. Blood pressure was 140/90; the pulse rate was 85 and regular. There were no murmurs. The old operative incisions were noted. Varicose veins of both lower legs were present.

Roentgenographic examination of the thorax at this time revealed an oval-shaped discrete mass on the right in the anterior mediastinum at the level of the hilus of the lung. Fluoroscopy showed a localized projection of the right anterior portion of the cardiac border starting at 1½ in. (3.8 cm.) above the diaphragm. It appeared to pulsate synchronously with the cardiac beat but was not considered to be a part of the ventricular wall. The kymographic films in the posterior-anterior and left anterior oblique directions showed some decrease of the amplitude

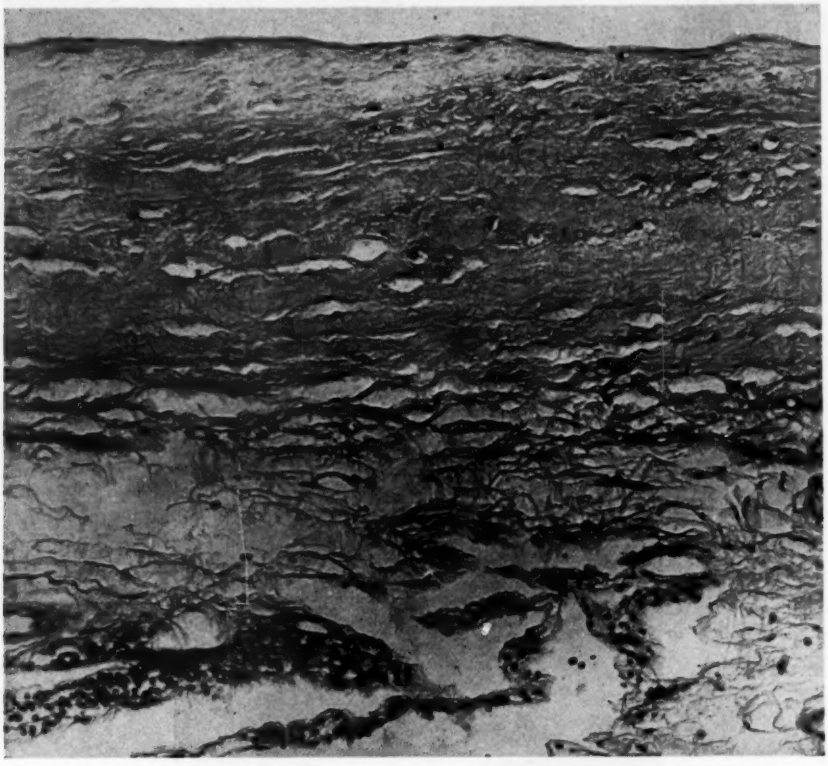

Fig. 3.—Photomicrograph, medium power, of wall of cyst. Nuclei of flat mesothelial cells which form a part of the lining of cyst are indistinct. Principal part of wall of cyst consists of hyalinized collagen which merges externally into adjacent fibrofatty and atrophic thymic tissue.

of the motion over the projection. The final roentgen diagnosis was a localized mass adjacent to the right anterior lateral border of the heart. A pericardial cyst was considered.

Routine laboratory tests were negative. There was no anemia.

On March 12, 1945, the right chest was opened through the bed of the sixth rib. A cystic tumor was found in the anterior mediastinum attached to the pericardium. There was no apparent communication between the cyst and the pericardial sac. The cyst was removed intact without difficulty.

Postoperatively the patient had an uneventful convalescence. She was discharged from the hospital 14 days after the thoracotomy, on March 26, 1945.

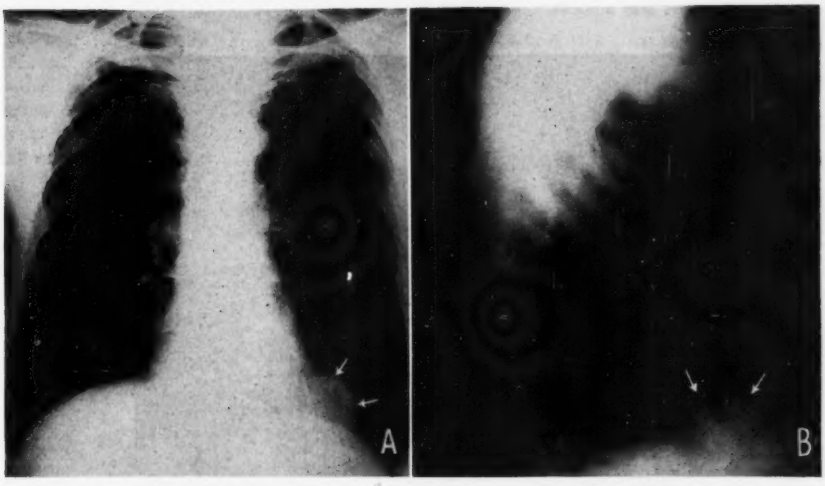


Fig. 4.—*A*, anterior view of chest, showing round tumor mass in cardiodiaphragmatic angle of left pleural cavity. *B*, lateral chest film demonstrating anterior position of same lesion (*A*).

Fig. 5.—Photograph taken at operation illustrates thin-walled cyst arising from mediastinum. There was no attachment to diaphragm or lung, but cyst lay adjacent to pericardium.

Gross pathological examination revealed the surgical specimen to be a thin-walled cyst 8 by 6 by 5 cm., filled with a clear watery fluid. The specific gravity was not measured. The lining of the cyst was smooth.

Fig. 6.—Photograph of opened cyst. Wall of cyst was transparent; lining was smooth and glistening. Clear straw-colored fluid was present in cyst.

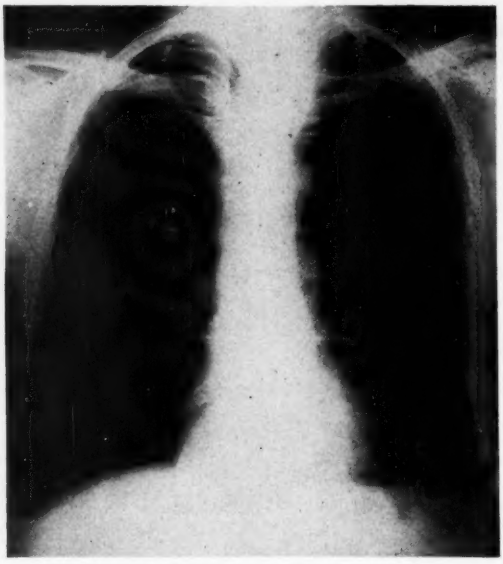

Fig. 7.—X-ray appearance of chest two weeks after surgical removal of cyst.

Sections for microscopic study [4] show that the wall of the cyst is composed principally of dense hyalinized connective tissue. The internal surface of the wall is partly lined by thin mesothelial cells, recognized more as elongated widely spaced nuclear structures than as definitive cells with detectable cytoplasm. The external surface of the wall of the cyst is

4. Microscopic study was done by Dr. G. M. Hass, Chairman, Department of Pathology, Presbyterian Hospital of Chicago.

attached by fibrous septa to adipose tissue and atrophic remnants of the thymus gland. There is no means by which the origin of the cyst can be defined, but its structure is consistent with that commonly encountered in cysts of pericardial origin.

CASE 2.—K. L., a 61-year-old white man, was admitted to the Presbyterian Hospital, Chicago, on Feb. 10, 1950. He had been under treatment for a peptic ulcer for many years. He had no symptoms referable to a tumor in the left cardiophrenic angle which had been diagnosed two years previously by roentgenography. The patient had experienced anginal attacks on occasions but refused medication.

Past surgical history included tonsillectomy, bilateral herniorrhaphy, and hemorrhoidectomy.

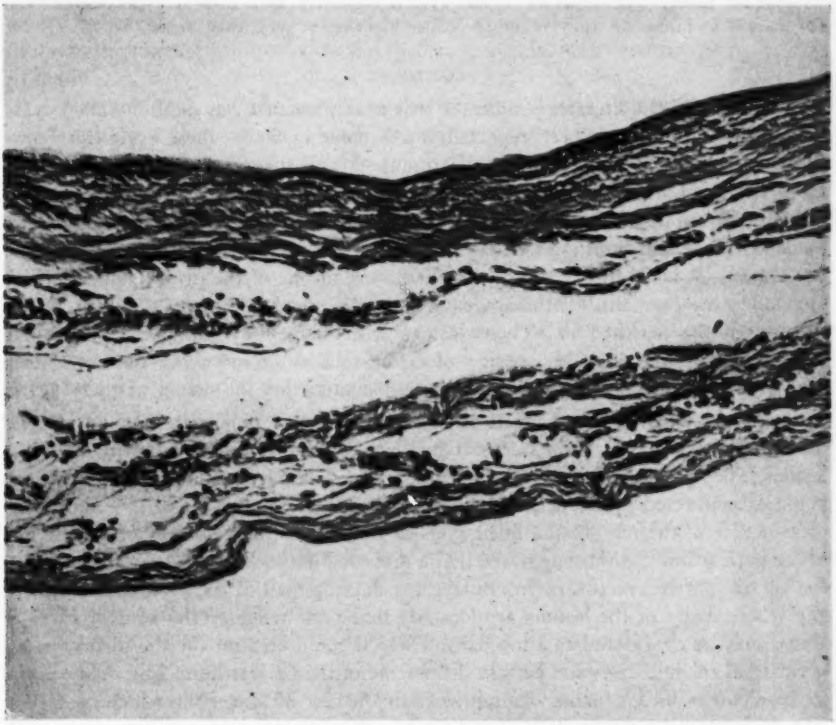

Fig. 8.—Photomicrograph, low power, of wall of cyst and contiguous pleura. There are no cells lining cyst. Wall is composed largely of parallel condensed bundles of collagen. A few strands of collagen traverse artifactual space between wall of cyst, and layer of pleura occupies lower one-half of microscopic field.

On physical examination the blood pressure was found to be 120/80; the pulse rate was 76 and regular. Examination of the heart and lungs was essentially negative. Roentgen examination of the thorax revealed a rounded area of increased density in the region of the left cardiophrenic angle anteriorly. There was no pulsation of this mass. Routine laboratory examinations were negative. No anemia was present.

At operation on Feb. 14, a large thin-walled cyst was found in the left cardiophrenic angle without any attachment to the diaphragm or to the lung. The apex of the cyst projected into the left pleural cavity, whereas the medial attachment of the cyst extended under the sternum almost to the midline. The cyst was adjacent to the pericardium but had no internal communication with the pericardial sac. The cyst was removed intact. The defect in the mediastinal pleura could be closed only partially.

The patient was discharged from the hospital on Feb. 22, 1950, after an uneventful postoperative course.

Gross pathological examination revealed the cyst to be a thin-walled structure about 6 cm. in diameter which contained a clear fluid. The cyst wall was unusually thin, gray, and translucent. The lining of the cyst was smooth.

Sections for microscopic study [4] show that the wall of the cyst is composed principally of parallel bundles of connective tissue. The internal bundles of collagen adjacent to the cavity of the cyst are fused and hyalinized. No nuclear or cytoplasmic structure indicative of a layer of lining cells can be recognized. The peripheral connective tissue of the wall of the cyst is separated from a thin layer of pleura or pericardium by occasional islands of fibroadipose tissue. The structure of this cyst is consistent with that of a pericardial cyst, but there is no means by which it can be defined as being of pericardial origin.

## COMMENT

A review of the literature indicates that a number of cases of thin-walled cysts of the mediastinum have been reported, but in some instances these cysts were confused with other lesions in the mediastinum. Many theories have been advanced as to the cause of these cysts. The close proximity to the pericardium suggests a derivation from that structure. Lambert [5] has stated that a knowledge of the development of the pericardium is essential to the understanding of the origin of some of these cysts. It is his theory that if there is failure of one of the primitive pericardial lacunae to merge with the others, a cavity persists which gives rise to a cyst in the vicinity of the pericardium. These lesions were named by Lambert "pericardial celomic cysts." Laipply [6] in a review of mediastinal cysts and cystic tumors agreed that Lambert had presented an adequate explanation for the origin of these cysts.

Lillie, McDonald, and Clagett have expressed the opinion that some process other than that proposed by Lambert might account for the development of these lesions. They pointed out that a number of these cysts are located at the cardiophrenic angle or connected to the pericardium by a pedicle; also, that there is a similarity of structure of the mesothelial-lined cysts of the mediastinum to that of diverticula of the pericardium. It was suggested that a diverticulum-like structure in the embryo, the ventral parietal recess, occurs during the development of the pericardium at the site where many of the lesions are located; that persistence of the ventral parietal recess may be considered as a mechanism which could account for the formation of pericardial celomic cysts and certain diverticula of the pericardium. The relationship of these two entities is further strengthened by the case of Mazer [7] in which the lesion was thought to be a cyst until it was demonstrated that fluid could be expressed beween it and the pericardium.

Further evidence of the relationship of pericardial cysts and diverticula of the pericardium is suggested in the case of a 26-year-old man with a true diverticulum of the pericardium reported by Bishop, Kirschner, and Pessar.[8] At operation a localized cystic mass was found adjacent to the left ventricle. The narrow neck of the cyst communicated with the pericardial sac. The histological picture was that

5. Lambert, A. V.: Etiology of Thin-Walled Thoracic Cysts, J. Thoracic Surg. **10**:1, 1940.

6. Laipply, T. C.: Cysts and Cystic Tumors of the Mediastinum, Arch. Path. **39**:153, 1945.

7. Mazer, M. L.: True Pericardial Diverticulum: Report of Case, with Safe Operative Removal, Am. J. Roentgenol. **55**:27, 1946.

8. Bishop, L. F., Jr.; Kirschner, P. A., and Pessar, T.: Diverticulum of the Pericardium, Circulation **1**:813, 1950.

of a pericardial cyst. Cushing [9] collected 39 cases of diverticulum of the pericardium from the literature and added one of his own. He felt that the basis of the so-called diverticulum in his patient was an inflammatory process. In 1951 Brown and Dunn,[10] in a review of lymphogenous cysts of the mediastinum, described the surgical removal of a pericardial cyst which was separated from the pericardium easily with the exception of one point where there was an intimate attachment. It was necessary to excise the adherent wall of pericardium with the cyst. A small opening was observed which connected the pericardial sac with one of the loculations of the cyst. It has been suggested that unequal development and partial coalescence of the embryological structures of the pericardium or congenital weakness of the pericardium with increased intrapericardial pressure result in a diverticulum or cyst formation.

Drash and Hyer, in an excellent review of this subject, discuss the suggestions and conclusions of Kindred as to the pathogenesis of these cysts. It is stated that the morphological evidence available suggests that the cysts originate by aberrant growth from the mesothelium of the pleural cavity as it invades the mesenchyme of the body wall. Such cysts could occur in any region of the pleura which has been derived from the secondary invasion of the body wall of the pleura. They hesitate to agree that these cysts are results of unabsorbed vesicles from which the pleural cavity is formed because these structures are too delicate and occur too early to contribute to the formation of these cysts. In view of the explanation of Kindred as to the origin of these cysts and as his opinion seems plausible to Drash and Hyer, they have recommended the term "mesothelial mediastinal cyst" as an applicable name to these cysts.

Nylander and Viikari [11] reported three cases of intrathoracic cysts arising from the diaphragm and located near the pericardium. Their opinion coincided with Broman's investigation that the so-called infracardiac bursa persists as a cyst. However, Drash and Hyer state that there is no need to conclude that cysts are derived from persistent infracardiac bursae or their abnormal outgrowths, because cysts derived from such sources would lie in the region of the esophagus, the central tendon region of the diaphragm.

In Butler's case, cited by Lambert, there was a thin-walled cyst in the anterior mediastinal diaphragmatic angle located adjacent to the pericardium but not attached to it. Its origin was considered extrapleural as it bulged into the pleural cavity covered by pleura. In a case reported by Laipply it was indicated that a large cyst occupying the angle between the diaphragm and the pericardium had a broad base attached to the pericardium. The lining of the cyst had no demonstrable epithelial lining in some places, whereas in others the cells were flattened.

In 1926, in the *British Journal of Surgery,* Edwards [12] described a large mediastinal cyst in a 30-year-old woman, which contained approximately 1½ to 2 pt.

9. Cushing, E. H.: Diverticulum of the Pericardium, Arch. Int. Med. **59**:56, 1937.

10. Brown, R. B., and Dunn, R. G.: Lymphogenous Cysts of the Mediastinum: Cystic Hygromas, Pericardial Cysts, and Pericardial Diverticulums, U. S. Armed Forces M. J. **2**:1651, 1951.

11. Nylander, P. E. A., and Viikari, S. J.: A Study of Intrathoracic Cysts Arising from the Diaphragm, Internat. Abst. Surg. **88**:140, 1949; in Surg., Genec. & Obst. Feb. 1949.

12. Edwards, A. T.: Intrathoracic New Growths: Account of 7 Operable Cases, Brit. J. Surg. **14**:607, 1926.

(750 to 1,000 cc.) of fluid. There was no apparent communication with the pericardium, but a dense attachment holding the cyst to the pericardium provided speculation as to whether the cyst was originally a primary diverticulum of the pericardium.

As an incidental finding at autopsy, Dufour and Mourrut [13] reported a thin-walled anterior mediastinal cyst arising from the parietal pericardium in an 86-year-old woman. This was called a "lymphatic cyst."

In 1931 Yater [14] reported an interesting case in the *American Heart Journal*. A 52-year-old man was thought to have an inoperable carcinoma of the stomach with metastases to the left lung. Above the dome of the diaphragm and partly overlapped by the shadow of the heart was a rounded shadow which was interpreted as a metastatic lesion in the lung or one associated with the heart. At autopsy

> projecting externally from the parietal pericardium at the apex and just above the diaphragm was a thin-walled, multilocular, ovoid cyst 4.5 cm. x 2.5 cm. This cyst was filled with clear watery fluid. The lining of the cyst was perfectly smooth. It was intimately associated with parietal pericardium and, undoubtedly, originated in it. The cyst was probably derived from a lymphatic vessel of the parietal pericardium. There was no evidence of adhesive pericarditis.

Churchill [15] reported a successful removal of a cyst of the mediastinum, which was called a "simple hydrocele of the mediastinum." The preoperative diagnosis was tumor of the pericardium. Mallory in the same discussion stated:

> I should assume that its lining was made up of the type of cell that one finds normally lining the pericardial and pleural cavities—the so-called mesothelium. These mesothelial cells are ordinarily present and can hardly be distinguished from endothelium, but they occasionally thicken up to a cuboidal type of cell that looks quite like epithelium.

Curreri and Gale,[16] employing artificial pneumothorax, described an anterior mediastinal tumor which was clearly defined as rounded and attached only to pericardium. Exploratory thoracotomy revealed a "simple serous cyst." They pointed out that these cysts differ from pericardial diverticula in that they arise on the left side of the pericardium and produce symptoms related to the gastrointestinal tract. In contrast, pericardial cysts occur on the right side and produce symptoms related to compression of the bronchus.

Greenfield and his associates [17] reported a case in which a 65-year-old man had difficulty in swallowing, anorexia, and loss of weight. A homogenous mass in the anterior superior mediastinum was found. At operation a thin-walled cyst lined with mesothelial cells was removed. The term "spring water" cyst was applied to the cyst because of the nature of the fluid within.

In a review of 109 tumors of the mediastinum, observed in Army personnel during World War II, Blades [18] stated that there were 10 instances of pericardial celomic cysts, all without symptoms. He pointed out that in the past some of these cysts may have been classified as cystic hygromas or cystic lymphangiomas.

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13. Dufour, H., and Mourrut.: Kyste de la partie supérieure du péricarde chez une femme de 86 ans, Bull. et mém. Soc. méd. hôp. Paris **53**:1482, 1929.

14. Yater, W. M.: Cyst of the Pericardium, Am. Heart J. **6**:710, 1931.

15. Churchill, E. D.: Cabot Case 23492: Simple Cyst of the Mediastinum, New England J. Med. **217**:958, 1937.

16. Curreri, A. R., and Gale, J. W.: Mediastinal Cysts, Ann. Surg. **113**:1086, 1941.

17. Greenfield, L.; Steinberg, I., and Touroff, A. S. W.: "Spring Water" Cysts of the Mediastinum: Case Report, J. Thoracic Surg. **12**:495, 1943.

18. Blades, B.: Mediastinal Tumors: Report of Cases Treated at Army Thoracic Surgery Centers in United States, Ann. Surg. **123**:749, 1946.

Lam,[19] in 1947, presented a most interesting report of a large anterior mediastinal cyst, diagnosed at the Henry Ford Hospital, in a 39-year-old woman who was followed elsewhere and was under observation for 10 years previously for so-called congenital heart disease. At operation a huge thin-walled cyst lying in the mediastinum anterior to the heart and great vessels was found. About 1 liter of straw-colored fluid was estimated to be present. The cyst had no epithelial lining. Recovery of the patient was uneventful.

In 1947 Leahy and Culver [20] reviewed a case in which a 50-year-old woman experienced severe symptoms, with hemoptysis, cough, and pain in the right lower chest. Preoperatively a dermoid cyst or hematoma had been suspected. At operation an orange-sized cyst, filled with clear fluid, was removed from the anterior mediastinum. The medial border of the cyst was in direct contact with the right margin of the pericardial sac.

In 1950 Drash and Hyer reported the successful removal of five mesothelial mediastinal cysts (pericardial celomic cysts of Lambert) and attempted to clarify some of the confusion associated with this infrequent lesion of the anterior mediastinum. In the same year, Lillie, McDonald, and Clagett described a series of their own cases of pericardial celomic cysts treated at the Mayo Clinic. These authors emphasized the part that the persistence of the ventral parietal recess of the pericardial celom may play in the development of these cysts and pericardial diverticula.

Reports in the past two years by Schein,[21] Buyers and Emery,[22] Kisner and Reganis,[23] Gillespie and Martinson,[24] Craddock,[25] Nichol and Dean,[26] and Rienhoff and his associates [27] indicate how much more frequently these pericardial celomic cysts have been found than the infrequent case described during the past 25 years. All authors describe a case in which thoracotomy resulted in successful removal of a cyst adjacent to the pericardium.

Recently, in a study of 101 patients with primary tumors or cysts of the mediastinum observed at The Johns Hopkins Hospital, Sabiston and Scott [28] reported two instances of pericardial cysts in the cardiophrenic angle and five cases of primary nonspecific mediastinal cysts; four of these cysts were located in the anterior mediastinum and one in the posterior mediastinum.

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19. Lam, C. R.: Pericardial Celomic Cysts, Radiology **48**:239, 1947.

20. Leahy, L. J., and Culver, G. J.: Pericardial Coelomic Cyst, J. Thoracic Surg. **16**:695, 1947.

21. Schein, C. J.: Cyst of the Pericardium, Am. J. Surg. **78**:411, 1949.

22. Buyers, R. A., and Emery, F. B.: Pericardial Celomic Cysts: Review of Literature and Report of Case, Arch. Surg. **60**:1002, 1950.

23. Kisner, W. H., and Reganis, J. C.: Pericardial Celomic Cyst with Symptoms, J. Thoracic Surg. **19**:779, 1950.

24. Gillespie, S. R., and Martinson, L. F.: Pericardial Celomic Cysts, Northwest Med. **49**:107, 1950.

25. Craddock, W. L.: Cysts of the Pericardium, Am. Heart J. **40**:619-623, 1950.

26. Nichol, W. W., and Dean, G. O.: Pericardial Celomic Cysts, U. S. Armed Forces M. J. **2**:473, 1951.

27. Rienhoff, W. J., Jr.; Jackson, R. L., and Moore, M. W.: Pericardial Coelomic Cysts: Review of Literature and Report of a Case, Bull. School Med. Univ. Maryland **36**:1, 1951.

28. Sabiston, D. C., Jr., and Scott, H. W., Jr.: Primary Neoplasms and Cysts of the Mediastinum, Ann. Surg **136**:777, 1952.

From the description of recorded cases of anterior mediastinal cysts, it seems that they may occur in the cardiophrenic angle or higher in the mediastinum. Of the 29 cases studied by Clagett and his associates, in 17 the cysts were at the cardiophrenic angle; in 7, connected to the pericardium by pedicles from the cardiophrenic angle, and in 5 the cysts were found at a higher level in the anterior mediastinum.

In most instances the recognition of these cysts has been accomplished by routine roentgenological examination of the chest in the absence of symptoms. If symptoms referable to the chest are present, they are vague and may include pressure over the heart, dyspnea, or coughing. Bronchograms and pneumothorax studies are valuable aids in diagnosis. The physician or general practitioner should not postpone consultation with a competent surgeon in the management and treatment of intrathoracic lesions of the mediastinum. Blades [29] has stated that the discovery of a mediastinal mass by roentgenographic examination with or without associated clinical manifestations demands positive diagnosis. If any doubt exists, the thorax should be explored. Harrington [30] has suggested that it is often impossible to determine with certainty the operability or type of tumor. Moreover, there is reason to believe that a benign tumor may undergo malignant change. Exploration is recommended in all cases of intrathoracic tumor unless the evidence indicates the existence of a hopeless situation. In addition, Alexander [31] has related that the "majority of circumscribed intrathoracic neoplasms arise within the lung; many of those that arise outside the lung are malignant and therefore prompt removal of any circumscribed neoplasm which cannot be proven benign is of vital importance."

Heuer [32] has stated that the mediastinum harbors an extraordinary variety of benign and malignant tumors. Bradford, Mahon, and Grow [33] have classified the various lesions found in the mediastinum, and the reader is referred to these publications for a thorough review of this subject.

A mediastinal cyst, especially in the cardiophrenic angle, presents the characteristic appearance of a rounded or oval-shaped area of increased density, adjacent to or confluent with the cardiac shadow. Good [34] has indicated that two-thirds of these pericardial celomic cysts are located in the anterior cardiophrenic angle. A lipoma, cyst of the pleura, or a diaphragmatic hernia at the foramen of Morgagni may be confused with these lesions. At operation a definite diagnosis of pericardial celomic cyst can be established rather easily.

Cysts located in the anterior mediastinum, higher than the lesions in the cardiophrenic angle, must be differentiated from other cystic tumors. Dermoid cysts and teratomas are encountered frequently. Embryonal cell rests from the alimentary tract, as well as the respiratory system, produce cystic lesions within the mediastinum. Adams [35] and his associates presented an excellent review of cases of broncho-

29. Blades, B.: Mediastinal Tumors, Editorial, Surg., Gynec. & Obst. **88**:131, 1949.

30. Harrington, S. W.: Surgical Treatment of Intrathoracic Tumors, Arch. Surg. **19**:1679, 1929.

31. Alexander, J.: Observations on Intrathoracic Neoplasms, Ann. Surg. **114**:734, 1941.

32. Heuer, G. J., and Andrus, W. DeW.: The Surgery of Mediastinal Tumors, Am. J. Surg. **50**:146, 1940.

33. Bradford, M. L.; Mahon, H. W., and Grow, J. B.: Mediastinal Cysts and Tumors, Surg., Gynec. & Obst. **85**:467, 1947.

34. Good, C. A.: The Mediastinal Shadow, Editorial, Surg., Gynec. & Obst. **96**:246, 1953.

35. Adams, W. E., and Thornton, T. F., Jr.: Bronchogenic Cysts of Mediastinum, with Report of 3 Cases, J. Thoracic Surg. **12**:503, 1943.

genic cysts of bronchial origin. Gastric mediastinal cysts, although rare, have been reported. These lesions histologically duplicate the lining of the stomach. Cystic lymphangiomas, resulting from a congenital malformation of the lymph channels, have multiple cavities and tend to be connected intimately with surrounding structures. Gross and Hurwith [36] reported on a 32-year-old man in whom at operation a large cyst, the size of two clenched fists, was found arising from the right side of the anterior mediastinum. It was slightly adherent to the pericardium and extended from the diaphragm well up to the level of the great vessels. The surgical specimen was characteristic of a cystic hygroma. A calcified cyst of the pericardium, the probable result of an injury to the chest, was reported by Dickson [37] in the *British Journal of Surgery*. Echinococcus cysts, occasionally located in the anterior mediastinum, must be considered. Primary tumors of the pericardium, though infrequent, are reported occasionally. Hochberg and Robinson [38] described the successful removal of a cavernous hemangioma of the pericardium in an 8-year-old child in whom the preoperative diagnosis was a pericardial cyst or an anterior mediastinal tumor. Samson [39] and his associates reported the surgical removal of mediastinal "tuberculomas" in four patients. These lesions are rare. There is uncertainty as to whether these granulomas are due to tuberculous or other organisms. Neurogenic tumors, tumors of the thymus gland, intrathoracic goiters, primary and secondary tumors of the mediastinal lymph nodes, and aneurysms of the aorta must be accounted for in the differential diagnosis of lesions of the mediastinum.

The clinical course in these cases depends upon the size and location of the cyst and whether symptoms are produced by pressure on adjacent structures. Infection may complicate the condition. Malignant changes can develop secondarily. Even though some cysts never produce symptoms, surgical removal is encouraged.

## SUMMARY

Two cases of thin-walled cysts of the mediastinum in close relationship to the pericardium are discussed. The mediastinal mass in the first patient was diagnosed originally as an aneurysm of the ascending aorta. Further observation and study prompted surgical exploration, identifying the mass as a benign mediastinal cyst which was successfully removed. In the second case a pericardial celomic cyst was suspected. Because of the patient's early reluctance to submit to surgery, exploration two years later confirmed the original diagnosis.

Much emphasis must be placed upon the importance of early diagnosis and the necessity for thoracotomy to establish the identity of cysts among other mediastinal tumors. The various conditions with which they are often confused are usually of a much more serious nature. Once the presence of a cyst is established, the ease of surgical excision is apparent. There should not be a period of watchful waiting once a mediastinal shadow on roentgenography leads one to suspect a mediastinal cyst or tumor.

36. Gross, R. E., and Hurwitt, E. S.: Cervicomediastinal and Mediastinal Cystic Hygromas, Surg., Gynec. & Obst. **87**:599, 1948.

37. Dickson, W.: Calcified Cyst of the Pericardium, Brit. J. Surg. **23**:612, 1936.

38. Hochberg, L. A., and Robinson, A. I.: Primary Tumor of the Pericardium Involving the Myocardium: Surgical Removal, Circulation **1**:805, 1950.

39. Samson, P. C.; Heaton, L. D., and Dugan, D. J.: Mediastinal "Tuberculoma": Surgical Removal in 4 Patients, J. Thoracic Surg. **19**:333, 1950.

# Case Reports

## POST-TRAUMATIC SUBDURAL HYDROMA

### Report of a Case of Massive External Hydrocephalus

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POST-TRAUMATIC external hydrocephalus is a relatively uncommonly recognized sequel of head injury.

Wycis,[1] in 1945, included an excellent review of the literature on this subject in his article in which he presented seven cases of post-traumatic subdural hydroma.

Cohen,[2] in 1927, described a patient who had a chronically recurring subdural collection of fluid and who, after several drainages were performed, finally underwent craniotomy. In this patient there was marked displacement of the brain and the ventricular system. This patient, however, was the only one found reported on in the literature in whom there was sufficient subdural fluid to cause deformity of the ventricular system.

A massive reaccumulating collection of subdural fluid which caused marked ventricular displacement was successfully treated by inserting a polyethylene tube intracranially to drain the subdural hydroma into the right mastoid antrum in the following patient.

#### REPORT OF A CASE

A 50-odd-year-old Negro man fell off a truck on Nov. 12, 1951. He had been unconscious for about half an hour following the accident. When seen on Nov. 19th, he was stuporous. The right pupil was larger than the left, and both reacted rather sluggishly to light. The left upper extremity was rather weak as compared with the right. This weakness was becoming increasingly severe, and he was becoming progressively drowsier.

Immediate bilateral trephinations were made in the temporal regions and when the dura was incised on the right side, xanthochromic fluid spurted out. Approximately 150 cc. of fluid was obtained from the right side and about 35 cc. from the left.

After this procedure the patient did well for a few days. The weakness of his left arm disappeared. He walked about the ward. A gradually enlarging swelling developed over the right temporal bony opening. The patient became progressively more drowsy and confused. He was next seen when transferred to the Mount Sinai Hospital at Miami Beach, on Dec. 29, 1951.

On admission he was rather drowsy, talked at times, but incoherently, and was alternately stuporous and restless. He was not oriented. He voided and defecated in bed, picked at the bedclothes, and pushed off those who tried to care for him.

1. Wycis, H. T.: Subdural Hydroma: A Report of 7 Cases, J. Neurosurg. **2**:340-357 (July) 1945.

2. Cohen, I., and Elsberg, C. A.: Chronic Subdural Accumulations of Cerebrospinal Fluid After Cranial Trauma: Report of a Case, Arch Neurol. & Psychiat. **18**:709-723 (Nov.) 1927.

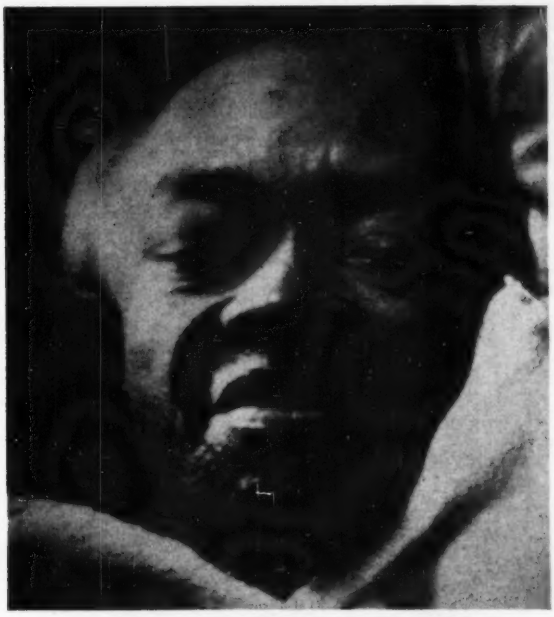

Fig. 1.—Preoperative appearance of patient.

Fig. 2.—Pneumoencephalogram, anteroposterior view taken with patient in upright position, using soft-tissue technique.

He moved all extremities, felt pinprick throughout. The reflexes were mildly hyperactive on the left. There was a large tense swelling under a healed linear incision in the right temporal region. This mass measured about 9 by 13 cm. (Fig. 1).

Lumbar puncture revealed crystal-clear cerebrospinal fluid under markedly increased pressure (over 500 mm. of water). The cerebrospinal fluid protein was only 25 mg. per 100 cc. The Kahn and colloidal gold reactions were normal.

After several drainages of 5 to 7 oz. (150 to 210 cc.) of cerebrospinal fluid had reduced the swelling, only to have it recur overnight despite pressure bandaging, it was elected to perform pneumoencephalography. This was done on Jan. 15, 1952. In the unusual soft-tissue technique film, the right temporal swelling was seen to contain fluid and air (Fig. 2).

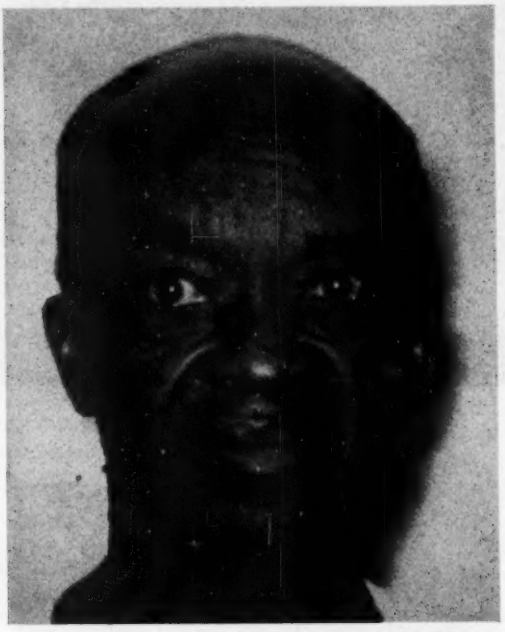

Fig. 3.—Postoperative appearance of patient.

On Jan. 17, the right temporal incision was reopened. The arachnoid was seen to be moderately thickened and opacified. There was a large collection of crystal-clear fluid in the subdural space. No evidence of a tear in the arachnoid could be seen. This incision was closed, and, through a separate incision placed just behind the right ear, a modified Nosik [3] procedure was carried out. A polyethylene tube was placed in a tantalum wedge to connect the right subdural space with the mastoid antrum of the same side.

His condition progressively improved. The temporal region on the right gradually became a concave pulsating decompression. The patient became oriented to time, place, and person (Fig. 3).

Now, 10 months postoperatively, the right temporal region is concave and pulsates. The patient cares for himself under supervision.

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3. Nosik, W. A.: Ventriculomastoidostomy: Technique and Observations, J. Neurosurg. **7**:236-239 (May) 1950.

## COMMENT

According to the literature,[4] the operative treatment of choice for subdural hydroma is bilateral trephination. This was carried out in the patient described, only to have the fluid reaccumulate. Repeated lumbar drainages of 5 to 7 oz. were of temporary decompressive value only—this despite the fact that there was direct communication between the lumbar subarachnoid space and the hydroma—as demonstrated by pneumoencephalography.

The magnitude of this patient's hydroma and its recurrence despite attempts at drainage therefore presented a special problem.

If a patient with a similar condition is encountered in the future, the drainage tube might be placed subcutaneously from subdural space to mastoid antrum to facilitate its removal.

## SUMMARY

A case of chronic subdural hydroma—external hydrocephalus—following trauma is presented.

A method of treatment of this condition is described.

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4. Dandy, W. E.: Chronic Subdural Hydroma and Serous Meningitis (Pachymeningitis Serosa: Localized External Hydrocephalus), in Lewis' Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1945, Vol. 2, pp. 291-293: Treatment of an Unusual Subdural Hydroma (External Hydrocephalus), Arch. Surg. **52**:421-428 (April) 1946. Gotten, N., and Hawkes, C. E.: Acute Subdural Hydromas, South. Surgeon **13**:689-695 (Sept.) 1947. Naffziger, H. C.: Subdural Fluid Accumulations Following Head Injury, J. A. M. A. **82**:1751-1752 (May 31) 1924. Svien, H. J.; Dodge, H. W., Jr., and Lake, C. L.: Ventriculo Mastoid Shunt in the Management of Obstruction to the Aqueduct of Sylvius in the Adult: Report of a Case, Proc. Staff Meet., Mayo Clin. **27**:215-218 (May 21) 1952.

# Clinical Notes, New Instruments and Techniques

## IMPROVED METHOD OF COLLECTING BILIARY DRAINAGE

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The usual method of collecting bile from a cholecystectomy or choledochostomy wound is to connect the drainage tube with a bottle attached to the bed or to the patient's dressings. When attached to the bed, ambulation is not practical. The usual bottles attached to the dressing are heavy and bulky. There is no standardization of methods of connecting the tube to the bottle. If tightly fitted, there is danger of pulling the tube out of the gall bladder or common duct by movements which might detach the bottle from the dressing.

To prevent accidental traction on the tube, we have adopted use of a special bottle and special connections.

A plastic, translucent, curved flask [1] (Fig. 1) is used for collecting bile. The flask is inconspicuous because of its shape, which fits the patient's body, and due to its light weight is more comfortable than a glass container; both these factors are greatly appreciated by ambulatory patients, particularly if the drainage tube is to be left in place for a considerable time. The flask is easily cleaned with warm water and is not stained by bile. A Lamb nipple [2] (Fig. 2) is slipped over the neck of the flask. A hole of such size as to accommodate the end of the drain without holding it tight is cut in the tip of the nipple. Minute holes, made with a narrow pocket-knife blade all around the base of the nipple, allow escape of air from the flask and thus prevent increased pressure in the container, created by accumulating bile. The nipple is equipped with a so-called fish-tail rubber valve (Fig. 2) which allows bile to flow into the flask but prevents its escape from the container when the drainage tube is disconnected and the flask is tilted. If any undue traction is exerted on the flask, the drain is automatically disengaged, and leakage results only from bile dripping from the tube but not from the container. Too much stress cannot be laid on the necessity of inserting the fish-tail valve through the neck of the flask in such a manner that it forms no kink, as this would stop the bile flow and have the same effect as clamping the tube.

After discharge from the hospital, when the patient can attach the flask securely to his underwear, it may be preferable to replace the nipple and the fish-tail valve by a rubber stopper equipped with two glass tubes. The end of the drain is attached to one tube, while the other serves as an air vent. When the flask is tilted, bile escapes through this air vent and soils clothing. To prevent this, one end of a short piece of rubber tubing is slipped over the air vent while the other end is attached with adhesive tape to the lower end of the flask (Fig. 2). This arrangement prevents bile spillage, irrespective of the position of the flask.

If desired, the plastic flask may be replaced by the bottom part of a gum rubber urinal,[3] available on the market (Fig. 3). This type of container is flat, flexible, and less conspicuous than a plastic flask, when worn by the ambulatory patient. The bag is equipped with a fish-tail valve, has a dependent outlet valve and can be attached to the drainage tube either firmly by

From the Surgical Service, St. Elizabeth Hospital.

1. The Parker Flask is distributed by Parker of London, Ltd., 660 Fifth Ave., New York 19.

2. The No. 97 Lamb nipple is manufactured by Davol Rubber Company, Providence 2, R. I.

3. The 4155 Davol Urinal Bottom, 14 oz. capacity, with No. 1812 connector, is manufactured by Davol Rubber Company, Providence 2, R. I.

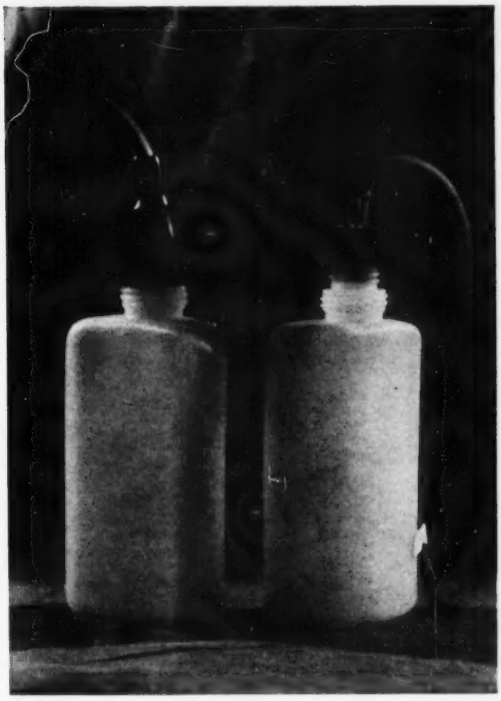

Fig. 1.—Left, plastic flask with Lamb nipple into which drain fits loosely; right, plastic flask with rubber stopper and air vent to which short piece of rubber tubing is attached.

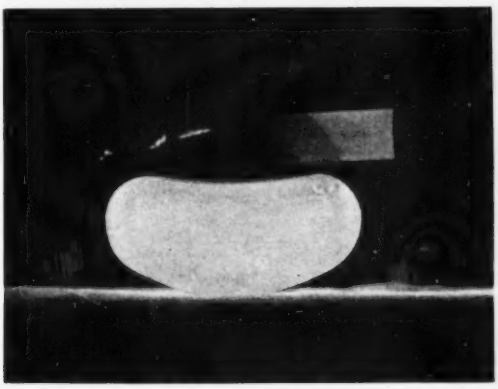

Fig. 2.—Lamb nipple with fish-tail valve placed on plastic flask. Note curved shape of flask.

means of a connector or loosely by means of a Lamb nipple. Perforations in the lower part of the nipple which act as air vents are not necessary because the container is flat, not rigid, and an increase of air pressure within it is prevented by gradual extension of the bag by accumulating bile.

Although considerably more expensive than the plastic flask, the bag requires no assembling of parts and eliminates the danger of a kink of the fish-tail valve which forms an integral part of the apparatus.

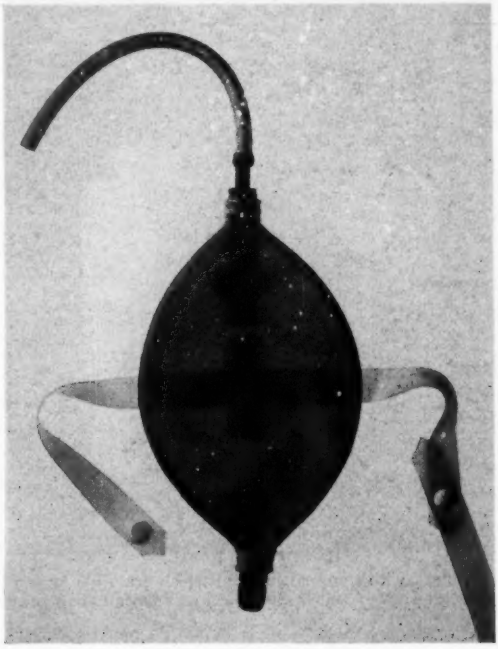

Fig. 3.—Bottom part of urinal which serves as bile collector is kept in place by strap. Drainage tube is attached to bag by means of connector. Fish-tail valve which hangs from neck of container is visible through translucent wall of bag.

If a loose connection between the drainage tube and the container is desired, as is usually the case during the early stages of the postoperative period, the rubber bag is preferable to the plastic flask. In later stages, when a firm connection is no longer objectionable, the flask may have a greater appeal to men patients because it can be worn in a trouser pocket, while the rubber bag is less conspicuous than a flask when hidden in a woman's garments.

## SUMMARY

A new method of collecting biliary drainage is based on the employment of a plastic flask or a portion of a rubber urinal as a bile collector. The device prevents bile spillage from the container and a premature slipping of the drain out of the wound.

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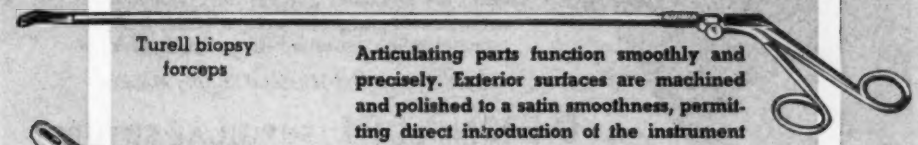

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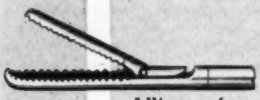
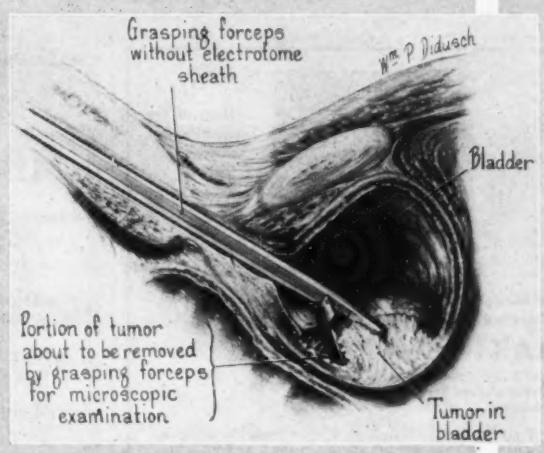


Alligator forceps


Grasping forceps without electrotome sheath
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Bladder
Portion of tumor about to be removed by grasping forceps for microscopic examination
Tumor in bladder

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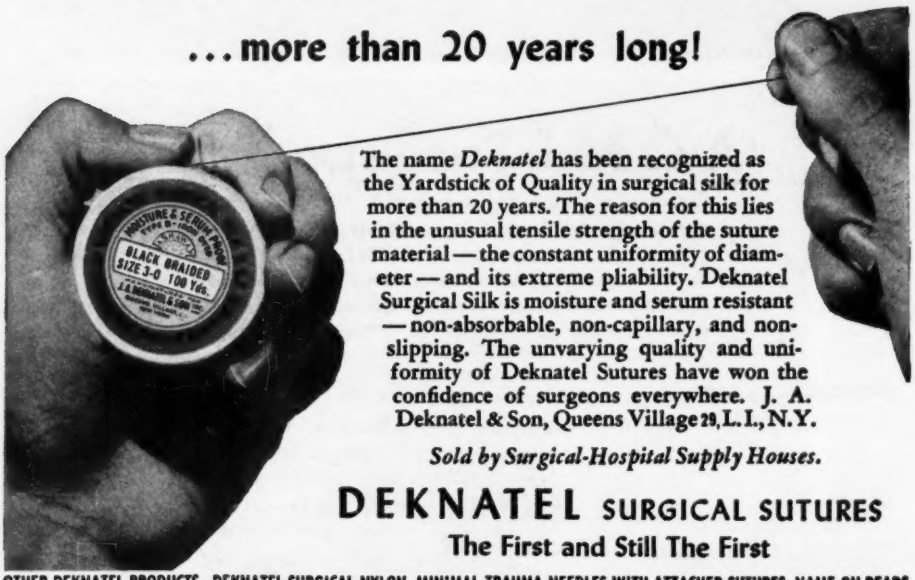


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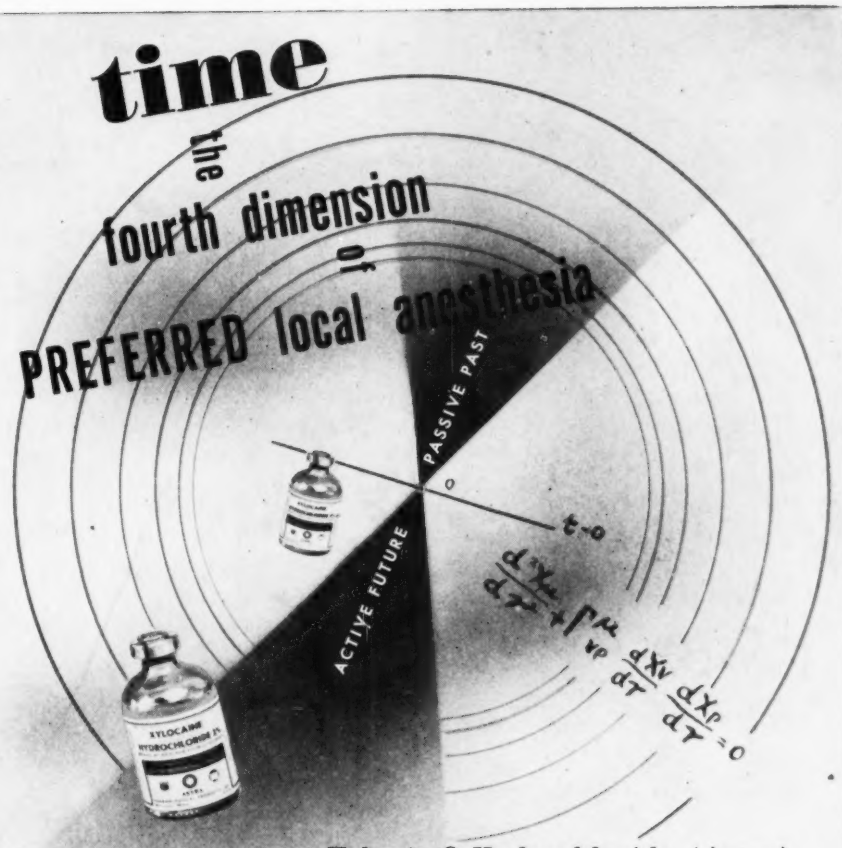


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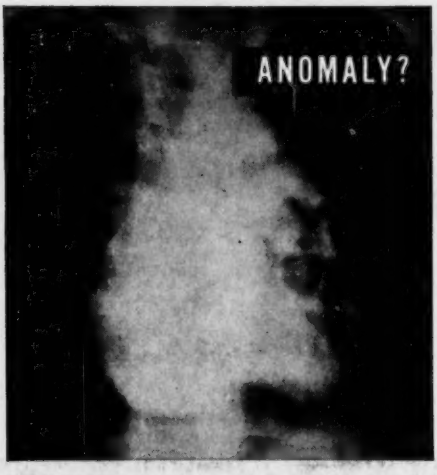


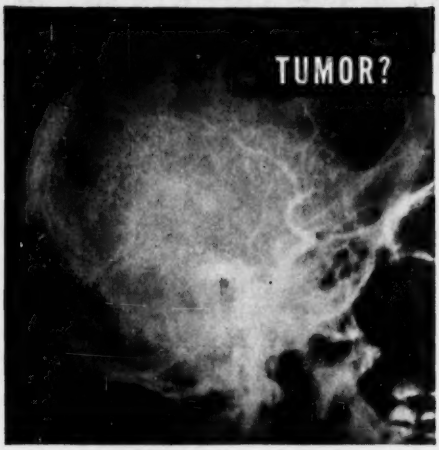


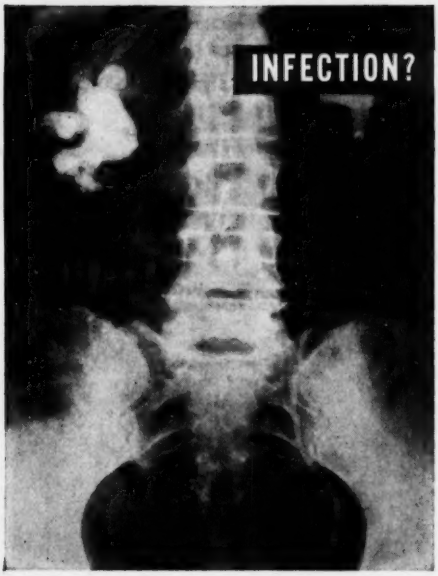


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